Clinical trial results:
The effect of curcumin and genistein in CF patients with a class III mutation

Summary

EudraCT number	2014-000817-30
Trial protocol	NL
Global end of trial date	08 May 2015

Results information

Result version number	v1 (current)
This version publication date	11 March 2020
First version publication date	11 March 2020

Trial information

Trial identification

Sponsor protocol code	TICTAC-2014

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UMC Utrecht
Sponsor organisation address	Lundlaan 6, Utrecht, Netherlands,
Public contact	Prof. dr. C.K. van der Ent, University Medical Center Utrecht, 0031 (0)887553201, k.vanderent@umcutrecht.nl
Scientific contact	Gitte Berkers, University Medical Center Utrecht, 0031 (0)887553741, g.berkers-3@umcutrecht.nl

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	01 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 May 2015
Global end of trial reached?	Yes
Global end of trial date	08 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Curcumin and genistein might be a cheap alternative for treating patients with a class III gating mutation

Main objective of the trial is to investigate the clinical response on treatment with curcumin and genistein in CF-patients with a class III S1251N mutation.

Protection of trial subjects:

N.A.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2014
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	Netherlands: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	4
Adolescents (12-17 years)	4
Adults (18-64 years)	5
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

inclusion criteria:
- CFTR genotype compound/ S1251N
- Already had a rectal biopsy to produce an organoid
- Male and female patients, aged 6 years or older on the date of informed consent or, where appropriate, date of assent
- Signed informed consent form (IC), and where appropriate, signed assent form

Period 1

Period 1 title	treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Treatment

Arm description:

treatment with curcumin and genistein

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

Dosage and administration details:

curcumin was dosed based on the weight of the patient with a minimum dose of 102.9 and maximum dose of 138.5 mg/Kg/day

Investigational medicinal product name	genistein
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dose was based on weight with a minimum dose of 3.3 and a maximum dose of 4.8 mg/Kg/day

Arm title	baseline

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Treatment	baseline
Started	13	13
Completed	13	13

Baseline characteristics

Reporting groups

Reporting group title	treatment period

Reporting group description: -

Reporting group values	treatment period	Total	
Number of subjects	13	13	
Age categorical 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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	15.0		
inter-quartile range (Q1-Q3)	10.0 to 33.0	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	8	8	

End points

End points reporting groups	
Reporting group title	Treatment
Reporting group description: treatment with curcumin and genistein	
Reporting group title	baseline
Reporting group description: -	

Primary: Sweat chloride concentration	
End point title	Sweat chloride concentration
End point description:	
End point type	Primary
End point timeframe: after 8 weeks of treatment	

End point values	Treatment	baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	76 (64 to 81)	80.0 (65.5 to 91.0)		

Statistical analyses

Statistical analysis title	Wilcoxon signed rank test
Comparison groups	baseline v Treatment
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.28
upper limit	41.72
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the first visit of the trial (t=0) untill the last visit (t= 8weeks)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	NA
Dictionary version	0

Reporting groups	
Reporting group title	treatment period
Reporting group description: during treatment with curcumin and genistein	

Serious adverse events	treatment period		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	treatment period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	5		
Vertigo			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Night sweats			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Gastrointestinal disorders			
Yellow stool			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	4		
Flatulence			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	3		
stomach ache			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	7		
diarrhea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
throwing up			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
cough up more sputum			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2014	The effect of curcumin and genistein was evaluated but not compared to the effect of Ivacaftor treatment. This was done in a separate trial

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported