Clinical trial results:
Modeling of lipoprotein in patients with familial hypercholesterolemia compared to healthy subjects

Summary

EudraCT number	2014-005473-36
Trial protocol	DE
Global end of trial date	05 February 2020

Results information

Result version number	v1
This version publication date	21 January 2021
First version publication date	21 January 2021

Trial information

Trial identification

Sponsor protocol code	Dezember2014Version2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1163-5436
Other trial identifiers	DRKS: DRKS00007125

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Freiburg, Institut für klinische Chemie und Laboratoriumsmedizin
Sponsor organisation address	Hugstetter Str 55, Freiburg, Germany, 79106
Public contact	medical director, Universitätsklinikum Freiburg, Institut für klinische Chemie und Laboratoriumsmedizin, +49 761 270 35160, karl.winkler@uniklinik-freiburg.de
Scientific contact	medical director, Universitätsklinikum Freiburg, Institut für klinische Chemie und Laboratoriumsmedizin, +49 761 270 35160, karl.winkler@uniklinik-freiburg.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2020
Global end of trial reached?	Yes
Global end of trial date	05 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective is to develope a mathematical model describing the lipoproteins of low density (LDL) in healthy probands and patients with familial hypercholesterinemia based on clinical data

Protection of trial subjects:

Study was part of regular patient treatment. Hence Protection=regular protection in patient treatment

Background therapy:

the protocol doesn't prescripe a background therapy

Evidence for comparator: -

Actual start date of recruitment	01 March 2015
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	Germany: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	0
Adults (18-64 years)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Time-span of recruitment: 09.10.2015 -05.02.2020
All patients were recruited in the lipid ambulance of the university hospital Freiburg, Germany

Pre-assignment

Screening details:

no screening, patients of the lipid ambulance of the university hospital Freiburg, Germany, who fulfilled the inclusion criteria were included (given written consent)

Period 1

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

Arms

Arm title	Atorvastatin

Arm description:

no Atorvastatin at baseline, start of Atorvastatin thearpy directly after baseline-visit. visite 1 (~12 weeks after baseline visit)

Arm type	Experimental
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	C10AA05
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

one 40mg tablet per day

Number of subjects in period 1	Atorvastatin
Started	12
Completed	6
Not completed	6
wrong sample treatment	1
Consent withdrawn by subject	2
Protocol deviation	3

Period 2	
Period 2 title	final visit
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Atorvastatin
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	C10AA05
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
one 40mg tablet per day

Number of subjects in period 2	Atorvastatin
Started	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	baseline

Reporting group description: -

Reporting group values	baseline	Total	
Number of subjects	12	12	
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	35.5		
inter-quartile range (Q1-Q3)	26 to 42	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	12	12	

End points

End points reporting groups

Reporting group title	Atorvastatin
Reporting group description:	
no Atorvastatin at baseline, start of Atorvastatin thearpy directly after baseline-visit. visite 1 (~12 weeks after baseline visit)	
Reporting group title	Atorvastatin
Reporting group description: -	

Primary: Difference of Apolipoprotein-B100 in LDL due to atorvastatin

End point title	Difference of Apolipoprotein-B100 in LDL due to atorvastatin
End point description:	
End point type	Primary
End point timeframe:	
3-6 month	

End point values	Atorvastatin	Atorvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: mg/dl				
median (inter-quartile range (Q1-Q3))	126.7 (112.2 to 144.8)	70.9 (59.6 to 87.7)		

Statistical analyses

Statistical analysis title	Wilcoxon signed rank test
Statistical analysis description:	
Check if Atorvastatin thearpy leads to the expected reduction in LDL Apolipoprotein B	
Comparison groups	Atorvastatin v Atorvastatin
Number of subjects included in analysis	12
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.028
Method	Wilcoxon (Mann-Whitney)

Primary: Estimation of the fractional catabolic rate (FCR) of Apolipoprotein B in LDL

End point title	Estimation of the fractional catabolic rate (FCR) of Apolipoprotein B in LDL

End point description:

estimation of FCR using a mathematical model based on the lipid composition of LDL and other lipoproteinfractions (especially HDL)

End point type	Primary

End point timeframe:

3-6 month

End point values	Atorvastatin	Atorvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: arbitrary				
median (inter-quartile range (Q1-Q3))	0.0065 (0.0007 to 0.0148)	0.0142 (0.0134 to 0.0338)		

Statistical analyses

Statistical analysis title	Wilcoxon signed rank test
Comparison groups	Atorvastatin v Atorvastatin
Number of subjects included in analysis	12
Analysis specification	Post-hoc
Analysis type	
P-value	= 0.028
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: during baseline and final visit (3-6 month)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0
Reporting groups	
Reporting group title	inflammation in the mouth
Reporting group description: inflammation in the mouth/tounge	

Serious adverse events	inflammation in the mouth		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (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	inflammation in the mouth		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Gastrointestinal disorders			
Inflammation	Additional description: inflammation in the mouth/tounge		
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30670016