Clinical trial results:
A Randomised Controlled Trial of Atorvastatin as an Anti-Inflammatory Agent in Non-Cystic Fibrosis Bronchiectasis in patients with Pseudomonas Aeruginosa (Atorvastatin 1)

Summary

EudraCT number	2010-022042-24
Trial protocol	GB
Global end of trial date	31 May 2017

Results information

Result version number	v1 (current)
This version publication date	01 August 2020
First version publication date	01 August 2020

Trial information

Trial identification

Sponsor protocol code	Atorvastatin 1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01299194
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ACCORD (University of Edinburgh & Lothian Healthboard)
Sponsor organisation address	47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
Public contact	Dr Pallavi Bedi, University of Edinburgh, +44 01312426662, drpallavibedi@gmail.com
Scientific contact	Prof Adam Hill, NHS Lothian, +44 01312421921, adam.hill318@nhs.net

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	10 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2012
Global end of trial reached?	Yes
Global end of trial date	31 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this randomised, double-blind controlled cross over study is to evaluate the efficacy of a 3 months treatment with atorvastatin versus placebo in patients with clinically significant bronchiectasis with colonisation with Pseudomonas aeruginosa.

Protection of trial subjects:

The study was conducted in accordance with all relevant data protection, ethical and regulatory requirements to ensure the privacy and security of patient information and to ensure the rights, safety and well-being of the patients and the quality of the research data.

Background therapy:

Excluded patients on a statin therapy.

Evidence for comparator: -

Actual start date of recruitment	14 March 2011
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	United Kingdom: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	13
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from a meeting that they were invited to in the Royal Infirmary of Edinburgh, where information regarding the trial was provided.

Pre-assignment

Screening details:

44 patients were screened for eligibility according to the protocol inclusion and exclusion criteria. 12 patients were excluded pre-randomisation: not meeting inclusion criteria (n = 9); declined to participate (n = 3); other reasons (n = 0).

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:

Unmatched placebo

Arms

Are arms mutually exclusive?	No
Arm title	Atorvastatin

Arm description:

Atorvastatin

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

Dosage and administration details:

1 tablet daily at night

Arm title	Placebo

Arm description:

Placebo

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

Dosage and administration details:

1 tablet daily at night

Number of subjects in period 1	Atorvastatin	Placebo
Started	16	16
Completed	13	14
Not completed	3	2
Discontinued intervention	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description:

Thirty-two patients chronically infected with P aeruginosa were recruited in this double-blind cross-over randomized controlled trial. Sixteen patients were recruited in each arm, were given atorvastatin 80 mg or placebo for 3 months followed by a washout period for
6 weeks, and then crossed over and administered the alternative therapy for 3 months.

Reporting group values	Overall trial	Total	
Number of subjects	32	32	
Age categorical 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)	0	0	
Adults (18-64 years)	13	13	
From 65-84 years	19	19	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	21	21	
Male	11	11	

End points

End points reporting groups

Reporting group title	Atorvastatin
Reporting group description: Atorvastatin	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Cough severity

End point title	Cough severity
End point description: Cough severity measured by Leicester Cough Questionnaire (LCQ). LCQ scores from 3 till 21, where a lower score means worse quality of life.	
End point type	Primary
End point timeframe: At the end of study - 3 months.	

End point values	Atorvastatin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: LCQ Score	16	16		

Statistical analyses

Statistical analysis title	Primary Outcome
Statistical analysis description: We used a two-sided paired test with a 5% level of significance, 80% power, and a mean of difference of 1.3. The sample size was 26 subjects. To account for an approximate 20% dropout rate, we recruited 32 patients. We analyzed the study with a modified intention-to-treat model. We did not take the washout period into account. To compare the proportion of patients with either clinical improvement (measured by the LCQ) or quality of life gains (measured by the SGRQ), we used a McNemar test.	
Comparison groups	Atorvastatin v Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.125 [2]
Method	t-test, 2-sided

Notes:

[1] - We analyzed the study with a modified intention-to-treat model. For demographic and clinical variables, we presented data as mean (SD) for continuous variables and number (%) for categorical variables, unless otherwise stated. To examine continuous variables, we calculated the change during the atorvastatin period (either baseline-3 months or 4-7 months) and compared this to the change during the placebo period (either 4-7 months or baseline-3 months] by a paired t test.

[2] - There was no evidence of a difference in the mean LCQ change in patients treated with atorvastatin compared with those treated with placebo (mean difference, 1.92; 95% CI, –0.57-4.41; P = .125).

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Within one week of the incident.	
Adverse event reporting additional description:	
Adverse events were reported to the sponsor on the sponsors SAE reporting form.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Atorvastatin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Atorvastatin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (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: 0 %

Non-serious adverse events	Atorvastatin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	
General disorders and administration site conditions			
Transient ischaemic attack			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2011	Protocol v3
21 October 2011	Protocol v4

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/29406231