Clinical trial results:
A randomised placebo controlled trial of rosuvastatin in systemic lupus erythematosus.

Summary

EudraCT number	2006-006214-16
Trial protocol	GB
Global end of trial date	16 May 2014

Results information

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

Trial information

Trial identification

Sponsor protocol code	Rosuvastatin

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01170585
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington Campus, London, United Kingdom, SW7 2AZ
Public contact	Dudley Pennell, Imperial College London, +44 (0)20 7351 8810, d.pennell@imperial.ac.uk
Scientific contact	Dudley Pennell, Imperial College London, +44 (0)20 7351 8810, d.pennell@imperial.ac.uk

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	04 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2014
Global end of trial reached?	Yes
Global end of trial date	16 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether Crestor will reduce the rate of progression of atherosclerosis in the carotid arteries of patients with systemic lupus erythematosus (SLE).

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2010
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	United Kingdom: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	33
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place in four London centers - Imperial College Healthcare NHS Trust (Hammersmith, Charing Cross and St Mary's Hospitals), and London Northwest Healthcare NHS Trust (Northwick Park Hospital). The cardiovascular magnetic resonance was performed at the Royal Brompton Hospital at baseline, 1 year and 2 years.

Pre-assignment

Screening details:

Thirty-nine patients were consented of whom thirty-three who fulfilled the eligibility criteria and were enrolled and randomised.

Period 1

Period 1 title	year 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received 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:

Daily 1 tablet for 2 years

Arm title	Rosuvastatin

Arm description:

Participants received Rosuvastatin

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

Dosage and administration details:

All patients uptitrated from an initial start dose of 5mg to 20mg rosuvastatin. Daily 1 tablet for 2 years

Number of subjects in period 1	Placebo	Rosuvastatin
Started	17	16
Completed	15	16
Not completed	2	0
Adverse event, non-fatal	2	-

Period 2

Period 2 title	Year 2
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received 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:

Daily 1 tablet for 2 years

Arm title	Rosuvastatin

Arm description:

Participants received Rosuvastatin

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

Dosage and administration details:

All patients uptitrated from an initial start dose of 5mg to 20mg rosuvastatin. Daily 1 tablet for 2 years

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Baseline reported for participants who started the 2. period.

Number of subjects in period 2[2]	Placebo	Rosuvastatin
Started	15	16
Completed	12	14
Not completed	3	2
Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline reported for participants who started the 2. period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Participants received placebo	
Reporting group title	Rosuvastatin
Reporting group description: Participants received Rosuvastatin	

Reporting group values	Placebo	Rosuvastatin	Total
Number of subjects	15	16	31
Age categorical Units: Subjects			
Adults (18-64 years)	15	16	31
Age continuous Units: years			
arithmetic mean	44.3	50.8	
standard deviation	± 14.4	± 12.9	-
Gender categorical Units: Subjects			
Female	15	14	29
Male	0	2	2
LDL cholesterol Units: mmol/L			
arithmetic mean	2.57	2.60	
standard deviation	± 0.41	± 0.56	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received placebo	
Reporting group title	Rosuvastatin
Reporting group description: Participants received Rosuvastatin	
Reporting group title	Placebo
Reporting group description: Participants received placebo	
Reporting group title	Rosuvastatin
Reporting group description: Participants received Rosuvastatin	

Primary: Changes in the Bilateral Carotid Artery Total Wall Volume Compared to Baseline

End point title	Changes in the Bilateral Carotid Artery Total Wall Volume Compared to Baseline
End point description:	
End point type	Primary
End point timeframe: Baseline, 1 year and 2 years	

End point values	Placebo	Rosuvastatin	Placebo	Rosuvastatin
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	15	12	14
Units: mm^3				
arithmetic mean (confidence interval 95%)	-83.65 (-159.41 to 7.89)	-53.35 (-111.86 to 5.16)	-78.20 (-169.89 to 13.48)	-64.66 (-136.86 to 7.53)

Statistical analyses

Statistical analysis title	Placebo vs Rosuvastatin in year 1
Comparison groups	Placebo v Rosuvastatin

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49
Method	t-test, 2-sided

Statistical analysis title	Placebo vs Rosuvastatin in year 2
Comparison groups	Placebo v Rosuvastatin
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	t-test, 2-sided

Statistical analysis title	Placebo vs Rosuvastatin with all time points
Comparison groups	Placebo v Rosuvastatin v Placebo v Rosuvastatin
Number of subjects included in analysis	53
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.42
Method	Mixed models analysis

Primary: The Bilateral Carotid Artery Distensibility

End point title	The Bilateral Carotid Artery Distensibility

End point description:

End point type	Primary

End point timeframe:

1 year and 2 years

End point values	Placebo	Rosuvastatin	Placebo	Rosuvastatin
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	16	12	15
Units: percentage				
arithmetic mean (standard deviation)	23.64 (± 9.76)	18.33 (± 5.07)	21.5 (± 8.02)	18.36 (± 7.39)

Statistical analyses

Statistical analysis title	Placebo vs Rosuvastatin in year 1
Comparison groups	Placebo v Rosuvastatin
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	t-test, 2-sided

Statistical analysis title	Placebo vs Rosuvastatin in year 2
Comparison groups	Placebo v Rosuvastatin
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	t-test, 2-sided

Statistical analysis title	Placebo vs Rosuvastatin all time points
Comparison groups	Placebo v Rosuvastatin v Placebo v Rosuvastatin
Number of subjects included in analysis	55
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.039
Method	Mixed models analysis

Secondary: Correlation of Vascular Findings to Ventricular Ejection Fraction

End point title	Correlation of Vascular Findings to Ventricular Ejection Fraction

End point description:

End point type	Secondary

End point timeframe:

2 year

End point values	Placebo	Rosuvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: correlation to carotid wall volume				
number (not applicable)	0.39	0.18		

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation of Vascular Findings to Ventricular Mass

End point title	Correlation of Vascular Findings to Ventricular Mass

End point description:

End point type	Secondary

End point timeframe:

2 years

End point values	Placebo	Rosuvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: correlation to carotid wall volume				
number (not applicable)	0.04	-0.15		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in LDL-C Lipids From Baseline

End point title	Changes in LDL-C Lipids From Baseline

End point description:

End point type	Secondary

End point timeframe:

1, year, 2 years

End point values	Placebo	Rosuvastatin	Placebo	Rosuvastatin
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	15	12	14
Units: mmol/L				
arithmetic mean (confidence interval 95%)	-0.08 (-0.38 to 0.22)	-1.00 (-1.40 to -0.6)	-0.14 (-0.47 to 0.2)	-0.61 (-1.06 to -0.16)

Statistical analyses

Statistical analysis title	Placebo vs Rosuvastatin in all time points
Comparison groups	Placebo v Rosuvastatin v Placebo v Rosuvastatin
Number of subjects included in analysis	53
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2 years	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

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

Serious adverse events	Placebo	Rosuvastatin	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)	4 / 16 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Cholecystectomy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Post-elective surgery bleeding			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgery for severe mitral regurgitation			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Lupusflare			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Costochondiritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Rosuvastatin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 17 (58.82%)	13 / 16 (81.25%)	
General disorders and administration site conditions			

General disorders subjects affected / exposed occurrences (all)	10 / 17 (58.82%) 26	13 / 16 (81.25%) 36	

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