# 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<br>Units: Subjects | | | |
| Adults (18-64 years) | 15 | 16 | 31 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 44.3 | 50.8 | |
| standard deviation | ± 14.4 | ± 12.9 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 15 | 14 | 29 |
| Male | 0 | 2 | 2 |
| LDL cholesterol<br>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<br>subjects affected / exposed<br>occurrences (all) | 10 / 17 (58.82%)<br>26 | 13 / 16 (81.25%)<br>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