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A 12-week, randomised, double-blind study evaluating the effects of low-dose (10 mg) and high-dose (80 mg) atorvastatin on macrophage activity and carotid plaque inflammation as determined by ultra small super-paramagnetic iron oxide (USPIO) enhanced carotid magnetic resonance imaging (MRI)

Submission date
03/03/2006

Recruitment status
No longer recruiting

Registration date
29/03/2006

Overall study status
Completed

Last Edited
10/09/2019

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00368589

Protocol serial number
N/A

Study information

Scientific Title
A 12-week, randomised, double-blind study evaluating the effects of low-dose (10 mg) and high-dose (80 mg) atorvastatin on macrophage activity and carotid plaque inflammation as determined by ultra small super-paramagnetic iron oxide (USPIO) enhanced carotid magnetic resonance imaging (MRI)

Acronym
ATHEROMA

Study objectives
This study will test the hypothesis that the treatment with atorvastatin 80 mg will demonstrate measurable changes in USPIO-enhanced MRI within the first three months of therapy. If this hypothesis is confirmed, this will provide additional clinical validation of USPIO-enhanced MRI methodology for the screening and the assessment of therapeutic response to anti-inflammatory interventions in patients with high-risk atherosclerotic lesions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
This study was approved by the Local Regional Ethics Committee, Cambridge, UK on 3/02/2006, reference number: 05/Q0108/441

Study design
Double blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Carotid atherosclerosis

Interventions
Patients with USPIO positive carotid plaques on MRI will be randomised into a high-dose or low-dose atorvastatin group. The high-dose statin group will receive 80 mg atorvastatin daily for 12 weeks and the low dose group will receive 10 mg atorvastatin. High resolution MRI will be performed at baseline, 6 weeks and at 12 weeks.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Atorvastatin

Primary outcome(s)
To establish whether inflammatory activity of the atherosclerotic plaque, as measured by USPIO-enhanced MRI, can be modified after the administration of high- or low-dose atorvastatin

Key secondary outcome(s))
1. To investigate MRI-derived tensile stress in carotid plaques following the administration of high- or low-dose atorvastatin
2. To quantify changes in cerebral micro-embolisation occurring in patients with carotid plaques treated with high- and low-dose atorvastatin
3. To investigate the effects of high- and low-dose atorvastatin on selected soluble plasma biomarkers
4. To compare macrophage content as determined by USPIO/MRI with histology in carotid atheroma plaques following the administration of high or low dose atorvastatin
5. To assess appearance of new lesions on brain MRI and correlate these with USPIO uptake in the carotid plaque and micro-embolic burden
6. To assess the pharmacokinetic parameters of atorvastatin

Completion date
01/04/2009

Eligibility

Key inclusion criteria
A subject will be eligible for inclusion in this study only if all of the following criteria are met:
1. Signed written informed consent prior to beginning study-related procedures (subject must understand the aims, investigational procedures and possible consequences of the study)
2. Male or female aged 18 to 80 years of age at screening. Female subjects must be of non-childbearing potential (post-menopausal females who have been amenorrheic >1 year, or pre-menopausal females with a documented hysterectomy or bilateral oophorectomy).
3. Positive USPIO-enhanced MRI of carotid plaque confirmed by a consultant neuroradiologist. This will be pre-defined.
4. Must either be statin naive or have been on a stable dose of a statin for ≥4 weeks prior to screening, with no evidence of statin intolerability

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
40

Key exclusion criteria
A subject will not be eligible for inclusion in this study if any of the following criteria apply:
1. Required continued use of non-statin lipid modifying therapies
2. History of statin intolerance
3. History of chronic viral hepatitis or other chronic hepatic disorders
4. Renal impairment
5. History of myopathy or inflammatory muscle disease
6. Doppler assessment of less than 40% stenosis during screening assessment
7. Contraindication to MRI scanning
8. Planned carotid surgery or endovascular intervention earlier than 10 weeks within the study period
9. Serum triglycerides >400 mg/dl (4.52 mmol/l) at screening
10. Patients with poorly controlled diabetes mellitus and hypertension
11. History of malignancy
12. Evidence of recent severe infection
13. Current life-threatening condition other than vascular disease
14. Alcohol or drug abuse within the past six months
15. Concomitant use of potent CYP450 3A4 inhibitors
16. Chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) and oral steroids therapy
17. Chronic use of immunosuppressants
18. Use of an investigational drug within 30 days or five half-lives (whichever is longer) preceding the first dose of study medication
19. Any other subject the investigator deems unsuitable for the study (e.g. due to either medical reasons, laboratory abnormalities, expected study medication non-compliance, or subjects unwillingness to comply with all study-related procedures)
20. Inability to give informed consent

Date of first enrolment
01/04/2006

Date of final enrolment
01/04/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Department of Radiology
Cambridge
United Kingdom
CB2 2QQ

Sponsor information

Organisation
GlaxoSmithKline (UK)

ROR
https://ror.org/01xsqw823

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline (GSK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2011		Yes	No
Results article	results	02/06/2009	10/09/2019	Yes	No