ISRCTN16590640 https://doi.org/10.1186/ISRCTN16590640

Study on the effects of rosuvastatin therapy on carotid plaque composition in asymptomatic patients enlisted to undergo carotid endarterectomy

Submission date
22/09/2017

Recruitment status
No longer recruiting

Registration date
03/10/2017

Overall study status
Completed

Last Edited
25/11/2020

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Atherosclerosis is a chronic condition when the arteries are clogged with plaque. There can be many complications of this condition including heart attacks and strokes. Treatment with medications that help lower the cholesterol in the blood known as statins (such as rosuvastatin) are able to prevent cardiovascular events in both primary and secondary prevention mainly because of a significant reduction of cholesterol. A growing body of evidence suggests that statin could also have additional treatment impacts such as having anti-inflammatory effects. The aim of this study was aimed to investigate the effects of short-term treatment with usual dose or a higher dose of rosuvastatin, one of the most potent statins available, on mechanisms known for influencing the biology of atherosclerotic plaque.

Who can participate?
Adults aged 50 to 85 years old who are high-risk for cardiovascular disease.

What does the study involve?
Participants are randomly allocated to one or two groups. Those in the first group receive the lipid lowering treatment with rosuvastatin either at the usual dosage (10 mg/day). Those in the second group receive the lipid lowering treatment with rosuvastatin at a high dose (40 mg/day). The medication is administered once a day (at 8 p.m.), according to the drug indication, for 12 weeks in order to achieve a plasma level of LDL-cholesterol <100 mg/dL at the time of endarterectomy (e.g. after 12 weeks of treatment).Participants are followed up at 12 weeks with blood tests.

What are the possible benefits and risks of participating?
Participants may benefit from a reduction in their risk for cardiovascular disease. There are no major risks with participating.

Where is the study run from?
1. University of L'Aquila (Italy)
2. SS. Filippo e Nicola Hospital (Italy)

When is the study starting and how long is it expected to run for?
January 2009 to August 2011

Who is funding the study?
University of L'Aquila (Italy)

Who is the main contact?
Professor Giovambattista Desideri

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number

QUASAR

Study information

Scientific Title
QUalitative Analysis of plaque Stability After Rosuvastatin therapy in asymptomatic patients enlisted to undergo carotid endarterectomy

Acronym
QUASAR

Study objectives
The aim of this study is to examine the effects of 2 different doses of rosuvastatin (10 and 40 mg /day) on mediator carotid plaque destabilization.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Public Health Agency of Avezzano-Sulmona, 06/15/2009, ref: protocol number 0040108/2019

Study design
Prospective single center randomised parallel group study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Patients clinically asymptomatic patients enlisted to undergo elective carotid endarterectomy for reducing long-term risk of stroke

Interventions
Participants are randomly allocated to one or two groups. Those in the first group receive the lipid lowering treatment with rosuvastatin either at the usual dosage (10 mg/day). Those in the second group receive the lipid lowering treatment with rosuvastatin at a high dose (40 mg/day).

The medication is administered once a day (at 8 p.m.), according to the drug indication, for 12 weeks in order to achieve a plasma level of LDL-cholesterol <100 mg/dL at the time of endarterectomy (e.g. after 12 weeks of treatment). Although such a reduction was the minimum for keeping the patient, a higher reduction with rosuvastatin has been aimed at.

Participants are followed up at 12 weeks with blood tests.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
1. MicroRNA expression in atherosclerotic plaques is measured using pre-costumed plates containing spotted microRNAs at week 12
2. RNA and/or protein levels of metalloproteinases, cholesterol transporters and other mediators of plaque destabilization in atherosclerotic plaques are measured using the western blot analysis at week 12
3. RNA and/or protein levels of potential target of deregulated microRNAs were measured using the western blot analysis at week 12

Key secondary outcome(s))
1. Plasma total cholesterol was measured using the electrochemiluminescence technology at 12 weeks
2. Plasma low density lipoprotein (LDL) is measured using the electrochemiluminescence technology at 12 weeks
3. Plasma high density lipoprotein (HDL) was measured using the electrochemiluminescence technology at 12 weeks
4. Plasma triglycerides was measured using the electrochemiluminescence technology at 12 weeks
5. Plasma glucose was measured using the electrochemiluminescence technology at 12 weeks
6. Plasma markers of inflammation such as CRP, sVCAM-1, sICAM-1, soluble E-selectin, soluble P-selectin were measured using enzyme immunoassay at 12 weeks

Completion date
11/08/2011

Eligibility

Key inclusion criteria
1. Clinical indication to the endarterectomy according to the international guidelines
2. Male or female patients between the ages of 50 and 85 years
3. LDL-cholesterol >100 mg/dl
4. Extracranial high-grade internal carotid artery (ICA) stenosis, near to carotid bifurcation
5. Patients have to be clinically stable at the time of randomization
6. High-risk patients, as defined by one or more of the following criteria:
6.1. Prior history > 4 weeks of cerebrovascular accident (CVA) or transient ischemic attack (TIA) consistent with North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria or prior history of amaurosis fugax occurring at any time.
6.2. Baseline hsCRP >2 mg/L
6.3. Echolucent plaque [Grey Scale Median (GSM) <25] on carotid ultrasound

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Sex
All

Total final enrolment
70

Key exclusion criteria
1. Chronic treatment with lipid-lowering agents including bile acid sequestrants, HMG-CoA-reductase inhibitors and nicotinic acid taken within 6 weeks and fibrates taken within 8 weeks of randomization, and probucol taken within 1 year of randomisation
2. History of statin induced myopathy, or serious hypersensitivity reaction to other HMG-CoA reductase inhibitors (statins) including rosuvastatin
3. Participation in another investigational drug study less than 4 weeks before enrolment in the study, or according to subjects local ethics committee requirements where a larger period is stipulated
4. Serum creatinine >176 mmol/L (2.0 mg/dL) or alternative threshold appropriate to study, to comply with label
5. Unexplained creatine kinase (CK 3xULN)
6. Current active liver disease (ALT/SGPT >2xULN) or severe hepatic impairment
7. History of alcohol or drug abuse within the last 5 years
8. Uncontrolled hypothyroidism defined as a thyroid stimulating hormone (TSH)>1.5 xULN
9. Nephrotic syndrome, anorexia nervosa or any other cause of secondary hyperlipidemia
10. History of malignancy (unless a documented disease free period exceeding 5-years is present) with the exception of basal cell or squamous cell carcinoma of the skin
11. Pregnant women, women who are breast feeding, and women of childbearing potential who are not using chemical or mechanical contraception or have a positive serum pregnancy test (a serum b-human chorionic gonadotrophin [β-HCG] analysis)
12. Patients on systemic immunosuppressive drugs including cyclosporine; systemic antifungal agents of the azole class including itraconazole and ketokonazole; erythromicin or clarithromycin; nefazodone; chronic systemic glucocorticoid therapy, or protease inhibitors
13. Partial ileal bypass
14. Any other condition or therapy, which, in the opinion of the investigator, might pose a risk to the patient or confound the results of the study
15. Poor mental function or any other reason to expect patient difficulty in complying with the requirements of the study
16. Treatment with any other investigational drug within 30 days prior to Visit 1
17. Patients not competent to give informed consent because of receptive language difficulty, intellectual decline, or psychiatric illness
18. Patients without clear and adequate selective angiographic visualization of the carotid arteries or their intracranial branches
19. Patients with carotid occlusive disease distal to the body of the second cervical vertebral body that is more significant than the surgically accessible lesion in the more prossimal portion of the artery
20. Patients with total internal carotid artery occlusion or carotid stenosis of less than 60%

21. Patients with previous cerebral infarction on either side of sufficient size to deprive the patient of all useful function in the affected territory
22. Patients who had a previous ipsilateral carotid endarterectomy

Date of first enrolment
20/07/2009

Date of final enrolment
15/12/2010

Locations

Countries of recruitment
Italy

Study participating centre
University of L'Aquila
Geriatric Unit
Via G. Di Vittorio, s.n.c.
Avezzano
L'Aquila
Italy
67100

Study participating centre
SS. Filippo e Nicola Hospital
Vascular Surgery Unit
Via G. di Vittorio
Avezzano
Italy
67051

Sponsor information

Organisation
University of L'Aquila

ROR
https://ror.org/01j9p1r26

Organisation

University of Chieti

Funder(s)

Funder type
Industry

Funder Name
ASTRAZENECA S.p.A., Basiglio (MI), via Francesco Sforza, Palazzo Volta, CAP 20080, Italy

Funder Name
Italian Ministry of University and Scientific Research (COFIN MIUR 2009, protocol number 2009L4X28T_002)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study is not expected to be made available. The dataset is held in the database of study investigators but they are not available since participants were not previously requested to authorize the sharing of their clinical informations with other research groups other than those of study investigators

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/01/2020	25/11/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes