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

Submission date	Recruitment status  No longer recruiting	<ul><li>Prospectively registered</li></ul>		
22/09/2017		☐ Protocol		
<b>Registration date</b> 03/10/2017	Overall study status Completed	Statistical analysis plan		
		[X] Results		
<b>Last Edited</b> 25/11/2020	Condition category Nervous System Diseases	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

### Contact name

Prof Giovambattista Desideri

### **ORCID ID**

https://orcid.org/0000-0002-0145-1271

# Contact details

Department of Life
Health and Environmental Sciences
University of L'Aquila
Coppito, L'Aquila
Italy
67100

# Type(s)

66100

Scientific

# Contact name

Prof Francesco Cipollone

# Contact details

Regional Center for the Study of Atherosclerosis, Hypertension and Dyslipidemia, "SS Annunziata" Hospital
Ce.S.I.-Met,
Geriatrics Clinic, Department of Medicine and Science of Aging
Chiety
Italy

# Additional identifiers

# Protocol serial number

# 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

# 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 [ $\beta$ -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

# 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