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European Carotid Surgery Trial 2

Submission date 05/07/2012	**Recruitment status** No longer recruiting	✓ Retrospectively registered ✓ Protocol added ? SAP not yet added – Results not yet expected – Raw data not yet expected ✓ Record updated in last year
Registration date 05/07/2012	**Overall study status** Ongoing	
Last Edited 21/09/2023	**Condition category** Circulatory System	

Plain English Summary

Background and study aims
Atherosclerotic carotid stenosis is a narrowing of the carotid artery in the neck by fatty deposits. It is an important cause of stroke, and hence disability and premature death. Previous studies have shown that an operation to remove the narrowing, known as carotid endarterectomy (CEA), is more effective than treatment with tablets to prevent stroke. In some patients a treatment called stenting may be as effective as surgery. Stenting involves a wire mesh tube being inserted via an artery in the groin and opened up across the narrowing in the neck. However, drug treatment has improved since the original studies of surgery. We think medical treatment is now so effective that the benefits of removing the narrowing may not justify the risk of surgery or stenting in patients with a lower risk of stroke, such as those who have had no symptoms for some months or never had symptoms from the narrowing. The aim of this study is to determine whether these patients should be managed by drug treatment alone or should still be referred for surgery or stenting.

Who can participate?
Patients over 18 years of age with atherosclerotic carotid stenosis and at a lower risk of stroke.

What does the study involve?
Participants have their medication adjusted to reach the recommended levels for cholesterol and blood pressure, and receive advice about healthy lifestyle. Half of the patients are randomly allocated to have surgery or stenting as soon as possible, and the other half continue on medical treatment alone until such time, if ever, that revascularisation surgery becomes clearly indicated. Participants are seen regularly for several years to check their cholesterol and blood pressure remain on target and to record any surgical complications and the occurrence of strokes or heart attacks.

What are the possible benefits and risks of participating?
The results will be used to help patients and doctors to choose which treatment plan is the safest and most effective. Both surgical endarterectomy and stenting carry a risk of causing a stroke at the time of the treatment. Previous studies showed a risk of stroke or death at the time of surgery or stenting of between 3 and 6 patients in every 100 patients. Treatment is not always successful and the carotid stenosis may recur and require further treatment or the artery may become blocked. A proportion of people treated with optimized medical treatment will also

suffer stroke at some time during follow-up despite treatment. Stroke caused by surgery, stenting or occurring during OMT may recover, cause permanent disablement or be fatal. Surgery also has a risk of causing a heart attack. About one in ten patients has cranial nerve palsy (temporary tongue or facial weakness). A haematoma (a solid swelling of clotted blood) may form at the site of incision, which may require removal. Angiography and stenting may also result in bruising or haematoma at the site of injection (usually in the groin) and can cause temporary discomfort or pain in the neck. There is a small risk of allergic reactions to the dye. The drugs used as part of OMT may cause adverse reactions or allergic reactions. The medical treatment that patients in both arms will receive will be carefully monitored and optimised with targets for control of blood pressure and lipid levels and advice on lifestyle. In the revascularisation group the surgeons and interventionists providing this treatment will have to show acceptable complication levels laid down in the protocol before their centre can be enrolled to randomise patients into the study. We have designed the protocol in such a way as to minimise risks to patients in both arms of the study and all patients should benefit from the optimisation and monitoring of their medical treatment.

Where is the study run from?
University College London, UK, University Hospital, Basel, Switzerland, and Amsterdam Medical Centre, The Netherlands.
(updated 10/11/2020, previously: The National Hospital for Neurology and Neurosurgery (UK))

When is the study starting and how long is it expected to run for?
March 2012 to March 2025

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Ekaterina Biggs
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Study website
http://www.ecst-2.com/

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Protocol/serial number
11034

Study information

Scientific Title
European Carotid Surgery Trial 2 (ECST-2): a randomised controlled trial

Acronym
ECST 2

Study hypothesis
Narrowing of the carotid artery in the neck by fatty deposits is an important cause of stroke, and hence disability and premature death. Previous trials have shown that an operation to remove the narrowing, known as carotid endarterectomy (CEA), is more effective than treatment with tablets to prevent stroke. In some patients a treatment called stenting where a wire mesh tube is inserted via an artery in the groin and opened up across the narrowing in the neck may be as effective as surgery. However, drug therapy has improved since the original trials of surgery. The trialists think medical therapy is now so effective that the benefits of removing the narrowing may not justify the risk of surgery or stenting in patients with a lower risk of stroke e.g. those who have had no symptoms for some months from the narrowing or never had symptoms. They propose a clinical trial to determine whether these patients should be managed by drug therapy alone or should still be referred for surgery or stenting.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Service Committee – East of England, Cambridge Central, 19/10/2011, ref: 11/EE/0347

Study design
Randomised controlled interventional trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Condition
Stroke

Interventions
Immediate endartorectomy and optimised medical therapy.

All patients will have their medication adjusted to reach recommended levels for cholesterol and blood pressure, and receive advice about healthy lifestyle. Half the patients will be randomly allocated to have surgery or stenting as soon as possible, the other half will continue on medical treatment alone until such time, if ever, that revascularisation becomes clearly indicated. Patients will be seen regularly for several years to check their cholesterol and blood pressure remain on target and to record surgical complications and the occurrence of strokes or heart attacks. An interim safety analysis will be performed using MRI follow up to assess rates of new cerebral infarction and haemorrhage.

Intervention Type
Mixed

Primary outcome measure
Any stroke at any time + non-stroke death within 30 days of endartorectomy

Secondary outcome measures
Added 06/05/2016:
The long-term rates of the following outcomes:
1. Ipsilateral stroke, confirmed/probable TIA, MI or any hospitalisation for vascular disease during follow up
2. Disabling stroke during follow up
3. New cerebral infarction or parenchymal haemorrhage on follow up MRI
4. Increase in white-matter changes on follow up MRI
5. Revascularisation during follow-up
6. Stenosis progression (defined as recurrent stenosis of the randomised artery after revascularisation, or progression in severity of stenosis in a non-revascularised artery)
7. The combination of stenosis progression or revascularisation during follow-up
8. Functional status as assessed by comparison of modified Rankin scale scores
9. The cost-effectiveness of carotid endarterectomy with OMT compared to OMT alone
10. Cognitive impairment or dementia during follow up reported by the investigator and measured by the Montreal Cognitive Assessment (MoCA)
11. Decline in functional status as assessed by an increase in the modified Rankin score (mRS)

12. Health-related quality of life and economic costs
Secondary analysis will also examine the risk factors for stroke, cognitive impairment and the other main outcome events during long term follow up (including the risks related to age, sex, symptoms, baseline brain imaging, centre and technique). In centres performing the relevant additional investigations, secondary analyses will examine the relationship between the main outcome events and baseline measures of plaque instability as determined by MR plaque imaging.

Overall study start date
23/03/2012

Overall study end date
31/03/2025

Eligibility

Participant inclusion criteria
1. Patients over 18 years of age with atherosclerotic carotid stenosis equivalent to at least 50% measured using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method
2. Patient is medically and neurologically stable and suitable for CEA or carotid artery stenting (CAS)
3. Patients with a carotid artery risk (CAR) score indicating a 5-year ipsilateral stroke risk of <20%. This may include patients with asymptomatic stenosis or symptomatic stenosis associated with features (e.g. delayed presentation) indicating intermediate or lower risk, confirmed by CAR Score <20%
4. Clinicians are uncertain about which treatment modality is best for the individual patient
5. Patient or appropriate representative is able and willing to give informed consent
6. Male and female participants

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
UK Sample Size: 200

Total final enrolment
429

Participant exclusion criteria

1. Patients (or their representatives) unwilling to have either treatment modality
2. Patients unwilling or unable to participate in follow up for whatever reason
3. Patients with a Rankin score greater than 3 for any reason. Such patients may be eligible for inclusion at such time as they improve to a Rankin score of 3 or less
4. Patients who are medically or neurologically unstable or have progressing neurological signs. Such patients may be eligible for inclusion at such time as they become stable
5. Patients in whom it is planned to carry out coronary artery bypass grafting or other major surgery within one month of carotid stenting or endarterectomy
6. Patients with a CAR Score >20% or other reason for believing the patient would get clear benefit from CEA or CAS
7. Patients not suitable for either surgery or stenting due to anatomical factors
8. Carotid stenosis caused by nonatherosclerotic disease e.g. dissection, fibromuscular disease or neck radiotherapy
9. Previous CEA or stenting in the randomised artery
10. Patients who are known to be pregnant
11. Patients who have a life expectancy of less than two years due to a preexisting condition e.g. cancer
12. Patients intolerant or allergic to all of the medications available for optimised modern medical therapy
13. Patients in clinical trials of medicinal products (CTIMPS) or who have been in a CTIMP within the last 4 months will not be enrolled
14. Patients in other trials (both stroke related and non stroke related) may be enrolled where this would not conflict with the treatments used in ECST2 or place undue additional burdens on the patient

Recruitment start date
23/03/2012

Recruitment end date
31/10/2019

Locations

Countries of recruitment
Canada

England

France

Germany

Italy

Netherlands

Scotland

Switzerland

United Kingdom

Study participating centre
The National Hospital for Neurology and Neurosurgery
London
United Kingdom
WC1N 3BG

Study participating centre
University College London Hospital
United Kingdom
NW1 2BU

Study participating centre
Sheffield Teaching Hospitals
United Kingdom
S10 2JF

Study participating centre
Nottingham University Hospitals
United Kingdom
NG5 1PB

Study participating centre
Universitätsklinikum Magdeburg
Otto-von-Guericke-Universität
Germany
-

Study participating centre
Leeds General Infirmary
United Kingdom
LS1 3EX

Study participating centre

Calderdale & Huddersfield NHS Foundation Trust
United Kingdom
HD3 3EA

Study participating centre
Frimley Park Hospital
United Kingdom
GU16 7UJ

Study participating centre
Academic Medical Centre, Amsterdam and Flevoziekenhuis, Almere
Netherlands
-

Study participating centre
East Kent University Hospital NHS Foundation Trust,
United Kingdom
CT1 3NG

Study participating centre
Royal Devon and Exeter Hospital
United Kingdom
EX2 5DW

Study participating centre
Albert Schweitzer Hospital Dordrecht
Netherlands
-

Study participating centre
St George's Healthcare NHS Trust
United Kingdom
SW17 0QT

Study participating centre

Manchester Royal Infirmary
United Kingdom
M13 9WL

Study participating centre
NHS Ayrshire & Arran
United Kingdom
KA27 8AJ

Study participating centre
Stroke Centre, University Hospital Basel
Switzerland
-

Study participating centre
Bradford Teaching Hospitals NHS Trust
United Kingdom
BD9 6RJ

Study participating centre
University Hospital North Durham
United Kingdom
DH1 5TW

Study participating centre
University Hospital South Manchester
United Kingdom
M23 9LT

Study participating centre
Erasmus Medical Centre Rotterdam
Netherlands
-

Study participating centre
Dalhousie University
Halifax

Canada
-

Study participating centre
Hospices Civiles de Lyon
Lyon
France
-

Study participating centre
University of Leipzig
Leipzig
Germany
-

Study participating centre
Verona University Hospital
Verona
Italy
-

Study participating centre
Kantonsspital St. Gallen
St. Gallen
Switzerland
-

Study participating centre
NSI-Lugano
Lugano
Switzerland
-

Study participating centre
Maastricht University Medical Centre
Maastricht
Netherlands
-

Study participating centre
Radboud University Nijmegen Medical Centre
Nijmegen
Netherlands
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Study participating centre
University Medical Center Utrecht
Utrecht
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Study participating centre
Ashford and St Peter's Hospitals NHS Foundation Trust
Lynne
United Kingdom
KT16 0PZ

Study participating centre
Pennine Acute Hospitals NHS Trust
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Sponsor information

Organisation
University College London (UK)

Sponsor details
Institute of Neurology
Queen Square
London
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Sponsor type
University/education

Website
http://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Stroke Association

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Funder Name
Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Alternative Name(s)
Schweizerischer Nationalfonds, Swiss National Science Foundation, Fonds National Suisse de la Recherche Scientifique, Fondo Nazionale Svizzero per la Ricerca Scientifica, Fonds National Suisse, Fondo Nazionale Svizzero, Schweizerische Nationalfonds, SNF, SNSF, FNS

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Publication of the main results will be submitted to a high-impact peer reviewed journal within one year after completion of randomisation and planned follow up.

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from the chief investigator Prof. Martin Brown.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		27/07/2022	28/07/2022	Yes	No