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Stopping or continuing blood thinners after stroke at young age without a known cause: STOP trial

Submission date 11/07/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 17/09/2024	**Overall study status** Ongoing	
Last Edited 17/01/2025	**Condition category** Circulatory System	

Plain English Summary

Background and study aims
In the Netherlands, 100,000 patients live with the long-term consequences of a TIA or ischaemic stroke at a young age (18-49 years old). The majority of these patients will use lifelong blood thinners (for example clopidogrel). This treatment strategy is based on studies among people with stroke due to atherosclerosis, who were on average 65 years of age. It is unknown whether lifelong use of blood thinners is effective for young people with TIA or ischaemic stroke as it is in elderly people, particularly in patients without a known cause for their stroke (cryptogenic stroke). Yet, young patients are exposed to blood thinners for decades with an increased risk of serious bleeding. It has never been established whether the benefits of blood thinners outweigh the risks for young patients, particularly in patients without atherosclerosis. The STOP trial aims to investigate whether blood thinners can safely be stopped three or more years after a TIA or ischemic stroke without a known cause at a young age.

Who can participate?
Patients who had a TIA or ischaemic stroke at the age of 18-49 years, for which the treating neurologist did not find a cause. The TIA or ischaemic stroke should have taken place at least 3 years before inclusion and participation in the study and patients should not have experienced a recurrent stroke or myocardial infarction afterwards.

What does the study involve?
Patients are randomly allocated to two groups: group 1 stops taking blood thinners, and group 2 continues taking blood thinners. Patients are requested to fill in a questionnaire each year. The study will run for 5 years.

What are the possible benefits and risks of participating?
Patients who stop using blood thinners have a lower risk of serious bleeding complications. In addition, stopping antiplatelet therapy provides convenience for patients who don’t have to take daily antiplatelet medication.

Patients who continue to use blood thinners have a risk of serious bleeding (for example bleeding from the gut or even bleeding in the brain). We expect that the risk of a recurrent stroke or myocardial infarction is similar for patients who stop or continue blood thinners. However, there might be a very small increased risk of a recurrent stroke or myocardial infarction among patients who stop blood thinners.

Where is the study run from?
The Radboud University Medical Center Nijmegen, the Netherlands

When is the study starting and how long is it expected to run for?
Recruitment is planned to start in october 2024 and run for two years

Who is funding the study?
The Netherlands Organisation for Health Research and Development

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2024-513092-40-00

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
114180, ZonMw Subsidy decision on file number: 10140252210002

Study information

Scientific Title
Stopping or continuing platelet inhibitors after cryptogenic stroke at young age: STOP trial

Acronym
STOP trial

Study hypothesis
Discontinuaton of antiplatelet drugs is non-inferior to continuation of antiplatelet durgs, three or more years after a cryptogenic stroke at young age

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/11/2024, METC Oost Nederland (Geert Grooteplein Zuid 10, Nijmegen, 6500 HB, Netherlands; +31243613154; metcoost-en-cmo@radboudumc.nl), ref: None provided

Study design
Multicenter randomized non-inferiority trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment, Safety

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

Condition
Patients with cryptogenic stroke at the age of 18-49 years

Interventions
Discontinuation of antiplatelet therapy.
The intervention is the discontinuation of oral daily antiplatelet therapy (clopidogrel 75mg once daily or acetylsalicylic acid 80mg once daily, with or without dipyridamole 200mg twice daily). The comparator is the continuation of antiplatelet therapy according to standard care. There is no specific trial drug manufacturer. Patients will be randomly allocated 1:1 by an external web-based system to the intervention or comparator arm.

Intervention Type

Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Clopidogrel, acetylsalicylic acid, dipyridamole

Primary outcome measure
Primary efficacy outcome:
1. A composite endpoint of major vascular events, defined as TIA with imaging confirmation, stroke, myocardial infarction, or death from vascular causes measured using a digital questionnaire or telephone follow-up and verified with medical records with annual follow-up for five years
Primary safety outcome:
2. Major bleeding, according to the International Society for Thrombosis and Haemostasis criteria, measured using a digital questionnaire or telephone follow-up and verified with medical records with annual follow-up for five years

Secondary outcome measures
The following secondary outcome measures are assessed using digital questionnaires or telephone follow-up with annual follow-up for five years:
1. Disability measured using the modified Ranking Scale
2. Quality of life measured using EQ-5D-5L
3. All cause mortality

Overall study start date
01/04/2024

Overall study end date
01/11/2032

Eligibility

Participant inclusion criteria
1. First ever ischaemic stroke, or TIA with evidence of ischaemia on imaging, 3-10 years before study participation
2. Age 18-49 years old at the time of TIA/ischaemic stroke
3. Cryptogenic aetiology, defined as no other aetiology after standard work-up according to national and international guidelines for young stroke (imaging of the brain (CT-scan or MRI-scan) and cervical arteries (CTA, MRA or carotid ultrasound), routine blood tests (complete blood count, erythrocyte sedimentation rate, CRP, antiphospholipid antibodies, ECG, at least 24 hours cardiac rhythm monitoring and transthoracic/transesophageal echocardiography).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
1316

Participant exclusion criteria
1. History of MI, coronary revascularisation or documented peripheral arterial disease
2. Other indication for antiplatelet therapy
3. Indication for oral anticoagulants or low molecular weight heparin
4. Recurrent ischaemic event at any time after the index event
5. Any stenosis of intracranial or cervical artery at time of stroke
6. Two or more risk factors for atherosclerotic disease prior to the index event, according to the following definitions:
6.1. Arterial hypertension (treated or known blood pressure before stroke >140/90 mm Hg)
6.2. Diabetes mellitus (treated or known blood fasting glucose >7 mmol/l)
6.3. Current smoking (or smoking stopped within the last 6 months)
6.4. Hypercholesterolaemia (treated or known low-density lipoprotein before the stroke >160 mg/dl or 4, mmol/l)
7. Any condition that prevents long-term follow-up

Recruitment start date
23/12/2024

Recruitment end date
01/10/2026

Locations

Countries of recruitment
Netherlands

Study participating centre
Radboud University Medical Center
Geert Grooteplein Zuid 10
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6500 HB

Sponsor information

Organisation
Radboud University Nijmegen Medical Centre

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
https://www.radboudumc.nl/EN/Pages/default.aspx

ROR
https://ror.org/05wg1m734

Funder(s)

Funder type
Research organisation

Funder Name
ZonMw

Alternative Name(s)
Netherlands Organisation for Health Research and Development

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Netherlands

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
01/11/2033

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date