Triple therapy prevention of Recurrent Intracerebral Disease EveNts Trial

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To determine the effectiveness of more intensive BP lowering provided by a *Triple Pill* strategy on top of standard of care, on the time to first occurrence of recurrent stroke after ICH.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON54804

Source
ToetsingOnline

Brief title
TRIDENT

Condition

- Central nervous system vascular disorders
- Vascular haemorrhagic disorders

Synonym
brain haemorrhage, Intracerebral haemorrhage

Research involving
Human

Sponsors and support

Primary sponsor: The George Institute for Global Health - Australia
Source(s) of monetary or material Support: National Health and Medical Research Council (NHMRC) van Australische overheid

Intervention

Keyword: Hypertension, Intracerebral Hemorrhage, Secondary prevention

Outcome measures

Primary outcome

- Primary outcome: Time to first occurrence of recurrent stroke, whether ischaemic or ICH.

- Secondary outcomes: Recurrent ICH; ischaemic stroke; fatal or disabling stroke; mortality; MACE [major adverse CV events of CV death, non-fatal myocardial infarction, or non-fatal stroke]; health-related quality of life [HRQoL] using the EuroQoL Group 5-Dimension Self-Report Questionnaire [EQ-5D]; physical function (simplified modified Rankin scale [smRS]); cognitive impairment, defined by standard cut-points on the Montreal Cognitive Assessments [MoCA].

Secondary outcome

see item primary study parameters/outcome of the study.

Study description

Background summary

Intracerebral haemorrhage [ICH] is the most serious and least treatable form of stroke, accounting for at least 10% of the 20 million new strokes in the world each year. Survivors are at high risk of recurrent ICH and other serious cardiovascular [CV] events. Whilst there is strong evidence that this risk can be reduced by lowering blood pressure [BP], many ICH patients do not receive any BP lowering treatment, and if they do, receive treatment such that their BP is inadequately controlled. TRIDENT has been designed to resolve persisting clinical uncertainty and provide definitive evidence on the effectiveness of more intensive BP lowering to prevent recurrent serious CV events after ICH

using a simplified combination regimen of BP lowering agents.

Study objective

To determine the effectiveness of more intensive BP lowering provided by a *Triple Pill* strategy on top of standard of care, on the time to first occurrence of recurrent stroke after ICH.

Study design

Multicentre, international, double-blinded, placebo-controlled, parallel-group, randomized controlled trial of a fixed low-dose combination BP lowering pill (Triple Pill) on top of standard of care, in patients with a history of acute ICH and systolic BP [SBP] levels defined as at least *high normal to borderline high* (defined as 130-160 mmHg) and on either minimal or no BP lowering treatment according to standard guideline definitions.
A 2-week, active run-in phase (in which all participants will receive the Triple Pill) will precede the double-blind treatment period to ensure the randomization of patients who tolerate the treatment regimen and procedures, thus increasing the likelihood of high adherence to the follow-up schedule.

Intervention

All participants who meet the eligibility criteria for the study will be randomized to:
1. Active treatment: encapsulation of generic regulatory approved combination of low doses of telmisartan 20mg, amlodipine 2.5mg, and indapamide 1.25mg (*Triple Pill*), or;
2. Control: encapsulation of 3 placebo tablets.

Study burden and risks

The main risks associated with this trial are (serious) adverse events caused by antihypertensive drugs (e.g. headache, syncope/collapse, falls, pedal oedema/ankle swelling, hyperkalaemia, hypokalaemia, hyponatraemia). It is currently uncertain which of the treatment strategies mentioned above is most effective and safe. The burden will consist of 5 visits in the first year, with two follow-up visits yearly thereafter.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Adults (>=18 years) with a history stroke due to primary intracerebral haemorrhage (ICH) confirmed by brain imaging, 2. Clinically stable, as judged by investigator, 3. Two resting systolic BP (SBP) levels, measured 5 minutes apart in the range 130-160mmHg recorded in a seated position., 4. Provision of written informed consent.

Exclusion criteria

1. Taking an ACE inhibitor antihypertensive drug that cannot be switched to any of the following alternatives:, - telmisartan 20 or 40mg, amlodipine 2.5 or 5mg, indapamide 1.25, or;, - an equivalent class (angiotensin receptor blocker, calcium channel blocker, or thiazide-like diuretic), or;, - a beta-blocker, 2. Contraindication to any of the study medications, in the context of currently prescribed BP lowering medication, 3. Unlikely/unable to complete the study procedures and/or follow-up, 4. Females of child bearing age and capability, who are pregnant or breast-feeding, or those not using adequate contraception, 5. Any condition that in the opinion of the responsible physician or

investigator that renders the patient unsuitable for the study (e.g. severe disability (ie modified Rankin Scale [mRS] score of 4-5] or significant memory or behavioural disorder or hyperkalaemia and/or hyponatremia, defined by local lab criteria)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-05-2018
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Placebo
Generic name:	Placebo
Product type:	Medicine
Brand name:	Triple pill
Generic name:	Fixed dose combination of telmisartan 20mg, amlodipine 2.5mg, and indapamide 1.25mg

Ethics review

Approved WMO Date:	31-10-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-12-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-06-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-10-2020

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-01-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-10-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-09-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-003724-23-NL
ClinicalTrials.gov	NCT02699645
CCMO	NL61790.091.17