# Acetazolamide in Aneurysmal Subarachnoid Hemorrhage

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Increased intracranial pressure and hydrocephalus |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50004

**Source**
ToetsingOnline

**Brief title**
ASH

### Condition

- Increased intracranial pressure and hydrocephalus
- Aneurysms and artery dissections

**Synonym**
hemorrhagic stroke, stroke, subarachnoid hemorrhage

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Radiologie
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Acetazolamide, Cerebral blood flow, Subarachnoid hemorrhage

## Outcome measures

### Primary outcome

Cerebral perfusion (arterial spin labeling (ASL) MRI) on day 7±2 after ictus.

### Secondary outcome

Cerebral perfusion (arterial spin labeling (ASL) MRI) on day 12±2 after ictus.

Serious adverse events (SAEs) and serious unexpected serious adverse reactions

(SUSARs) until 10 weeks after ictus.

The occurrence of DCI. DCI will be defined as either *clinical deterioration or

cerebral infarction due to delayed cerebral ischemia*.

# Study description

### Background summary

Approximately 30% of patients with subarachnoid hemorrhage (SAH) suffer from delayed cerebral ischemia (DCI). This in-hospital complication increases the risk of poor functional outcome. The only available drug that reduces the risk of DCI is nimodipine. However, the effect of nimodipine is only modest. Acetazolamide, a carbonic anhydrase inhibitor, could be a useful additional drug for the prevention of DCI by acting on 3 different pathways: (1) it increases cerebral blood flow via vasodilation, (2) it decreases brain edema through carbonic anhydrase inhibition, and (3) it decreases cerebrospinal fluid production. These combined actions of acetazolamide make it a promising drug for the prevention of DCI in patients with SAH.

### Study objective

In a phase II study we will evaluate safety and proof-of-concept of acetazolamide in patients with aneurysmal SAH. The primary aim of this study is to evaluate whether acetazolamide improves cerebral perfusion as measured with magnetic resonance imaging (MRI) performed 7±2 days after ictus. The secondary objectives of this study are to investigate (1) the safety of acetazolamide

when given until day 14 after aneurysmal SAH (aSAH), (2) whether acetazolamide improves cerebral perfusion also at day 12±2 after ictus, (3) whether the proportion of patients with DCI is lower in the intervention group. The tertiary objectives of this study are: (1) to investigate whether acetazolamide improves the Quality of Life score and modified Rankin Scale (degree of disability) at 10 weeks after SAH, and (2) to examine whether the proportion of patients with hydrocephalus is lower in the intervention group.

## Study design

This study will be an intervention study with a PROBE design (Prospective, Randomized, Open-label study with Blinded End-point assessment) to evaluate the safety and proof of concept of acetazolamide in patients with aneurysmal SAH. The participant and treatment team will be open to group assignment, and the researcher performing the data analysis will be blinded.

## Intervention

In the intervention group, subjects will receive acetazolamide intravenously as well as treatment as usual. The dosage of acetazolamide will be similar to the average dosage used for the treatment of intracranial hypertension: 1.5 grams per day in three dosages of 0.5 grams in a 100 mL solution per dose. The intervention will be initiated within 120 hours after ictus, after aneurysm securing, and it will be continued until day 14 after ictus in addition to the usual treatment. The control group will not receive any study medication and will only receive treatment as usual.

## Study burden and risks

The patients included in this study will undergo two MRI scans for the purpose of the trial and they will receive either acetazolamide in addition to standard clinical care or only standard clinical care. Treatment group will be randomly assigned. There is no risk related to the MRI in this patient population and no contrast agents (such as gadolinium) will be used. Patients in whom acetazolamide is administered nearly always experience harmless side effects such as tingling in the fingers, toes, and perioral region. A less common side effect is malaise. Severe side effects are rare, and occur in 0.01-1% (see Appendix 1). Rare side effects (frequency 1/100 - 1/10.000) include toxic skin manifestations and hematological changes. All patients visit the UMC Utrecht for neuropsychological testing at 10 weeks as part of standard clinical care. At this visit, an additional 10 minute Quality of Life questionnaire will be performed by the neuropsychologists. There is no risk related to the Quality of Life questionnaire in this population. The modified Rankin Scale is administered as part of standard clinical care during the neuropsychological testing.

# Contacts

**Public**
Selecteer

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**Scientific**
Selecteer

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

>=18 years old
Aneurysm confirmed by the presence of subarachnoid blood by computed tomography (CT) or lumbar puncture and by visualization of the aneurysm on either CT angiography, MR angiography or digital subtraction angiography
Hospital arrival <=120 hours of ictus
Adequate treatment of the aneurysm

## Exclusion criteria

Intensive care (IC) required for >120 hours after ictus (i.e., during inclusion window)
Perimesencephalic bleeding

Traumatic SAH
Severe liver dysfunction or severe renal dysfunction
Allergic reaction for sulfomides
Any contraindication for MR imaging (e.g. metal objects within or around the body)
Pregnancy or women who are breastfeeding
Addison*s disease
Phenytoin use

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Single blinded (masking used) |

**Primary purpose:** Treatment

## Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 16-01-2018 |
| Enrollment: | 40 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | DIAMOX |
| Generic name: | Acetazolamide |
| Registration: | Yes - NL outside intended use |

# Ethics review

Approved WMO

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|---|---|
| Date: | 15-05-2017 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 02-08-2017 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 10-01-2018 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 08-08-2018 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 05-12-2018 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 13-03-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 23709
Source: Nationaal Trial Register
Title:

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2016-005151-25-NL |
| CCMO | NL60773.041.17 |
| Other | nog in behandeling |
| OMON | NL-OMON23709 |

# Study results

Date completed: 12-07-2019

Results posted: 17-01-2024

**Summary results**
Trial ended prematurely

**First publication**
01-03-2021