

# Cerebrovascular reserve and white matter disease in patients with chronic anemia

Gepubliceerd: 20-03-2019 Laatste bijgewerkt: 18-08-2022

relationship between CVR, CB, and vascular/inflammatory markers Co-localization of white matter damage and regions of low CVR Global and regional response of CVR to simple transfusions, exchange transfusions and hydroxyurea.

|                             |                       |
|-----------------------------|-----------------------|
| <b>Ethische beoordeling</b> | Positief advies       |
| <b>Status</b>               | Werving gestart       |
| <b>Type aandoening</b>      | -                     |
| <b>Onderzoekstype</b>       | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON27211

### Bron

NTR

### Verkorte titel

IMPROVE

### Aandoening

Sickle Cell Disease, Thalassemia

### Ondersteuning

**Primaire sponsor:** AMC

**Overige ondersteuning:** No funding

### Onderzoeksproduct en/of interventie

### Uitkomstmaten

#### Primaire uitkomstmaten

relationship between CVR, CB, and vascular/inflammatory markers  
Co-localization of white matter damage and regions of low CVR  
Global and regional response of CVR to simple transfusions, exchange transfusions and hydroxyurea.

## Toelichting onderzoek

### Achtergrond van het onderzoek

Low haemoglobin levels raise resting cerebral blood flow (CBF) and leave patients with inadequate cerebrovascular reserve (CVR). As a result, impaired CVR represents the strongest risk factor for white matter injury, volume loss, and stroke. The main goal of this project is to identify CVR predictors including CBF, age, sex and vascular stressors in anaemic and control subject using several MRI techniques. While anaemia is correlated with other cerebrovascular risk factors in the general population (hypertension, kidney disease, chronic inflammation, heart failure), we assume that anaemia, by decreasing CVR, created and increased vulnerability to white matter damage in patients with Sickle Cell Disease (SCD). Through the use of simple and exchange transfusions in selected patients with SCD and thalassemia, we will study the relative importance of haemoglobin S% and total haemoglobin level on regional CVR. We will identify other modifiable risk factors (iron overload, vascular inflammation) that may impair CVR. By comparing CVR and white matter damage across a broad spectrum of SCD and thalassemia syndromes, we will be able to separate the damaging effects of haemolytic anaemias in general from damage specific to sickle haemoglobin.

### Doel van het onderzoek

relationship between CVR, CB, and vascular/inflammatory markers  
Co-localization of white matter damage and regions of low CVR  
Global and regional response of CVR to simple transfusions, exchange transfusions and hydroxyurea.

### Onderzoeksopzet

2 MRIs

### Onderzoeksproduct en/of interventie

Blood draw, Neurocognitive tests, infusion placed. ECG leads or pulse unit placed, 15 minutes structural MRI, 15 min Functional MRI pre-ACZ, administration of ACZ, 15 min ASL assesses time course, 15 min functional MRI post ACZ.

## Contactpersonen

### Publiek

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### Wetenschappelijk

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Patient group:  
Sickle cell disease,  
Thalassemia major, thalassemia intermedia, and HbH disease  
18 years of age or older  
Informed consent

Control Group:  
Either AS or AA haemoglobin  
18 years of age or older  
Informed consent

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Patient group:  
Hospitalization in the past month for any reason  
Inability of the patient to provide informed consent  
Contraindications for MRI, such as claustrophobia or the presence of metal in the body  
Sickle cell crisis at the moment of participation up to one month prior to participation  
History of cerebral pathology that compromised measurements, such as cerebral palsy, brain

tumour, meningitis, overt infarct  
Brain surgery performed in the last 3 months

ACZ contraindications  
Severe liver, heart or renal dysfunction (clearance <10 mL/min)  
Allergy to sulphonamide  
Pregnant or breastfeeding  
Use of phenytoin, procaine or acetylsalicylic acid  
Risk of hypokalaemia  
Addison's disease  
Severe asthma or emphysema

Control Group:  
Any known chronic illness that may compromise subject safety or data integrity.  
Vascular risk factors  
Hypercholesterolemia  
Contraindications for MRI  
Contraindications for ACZ  
Developmental delay, stroke, seizure disorder, or neurological conditions other than simple migraine  
inability to cooperate with MRI examinations  
Diabetes  
Uncontrolled hypertension or history of hypertension

## Onderzoeksopzet

### Opzet

|                  |                         |
|------------------|-------------------------|
| Type:            | Interventie onderzoek   |
| Onderzoeksmodel: | Factorieel              |
| Toewijzing:      | Niet-gerandomiseerd     |
| Blinding:        | Open / niet geblindeerd |
| Controle:        | Geneesmiddel            |

### Deelname

|                         |                      |
|-------------------------|----------------------|
| Nederland               |                      |
| Status:                 | Werving gestart      |
| (Verwachte) startdatum: | 15-08-2018           |
| Aantal proefpersonen:   | 140                  |
| Type:                   | Verwachte startdatum |

## Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

### Ethische beoordeling

Positief advies

Datum: 20-03-2019

Soort: Eerste indiening

### Registraties

#### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

#### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register       | ID                       |
|----------------|--------------------------|
| NTR-new        | NL7620                   |
| Ander register | METC AMC : METC 2018_215 |

### Resultaten