# Reducing the incidence of daily life pain in patients with sickle cell disease

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Haemoglobinopathies |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON39603

**Source**
ToetsingOnline

**Brief title**
NAC Trial

### Condition

- Haemoglobinopathies

**Synonym**
Sickle cell pain; painful crisis

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** ZON NW

## Intervention

**Keyword:** crisis, N-Acetycysteine, Oxidative stress, Sickle cell disease

## Outcome measures

### Primary outcome

The frequency sickle cell-related pain in daily life

### Secondary outcome

- The severity of sickle cell related pain in daily life.

- The frequency and severity of painful crises in daily life.

- The frequency and severity of hospital admission for painful crises

- The health related quality of life,

- Societal costs of SCD related care

- Hematological markers of oxidative stress, hemolysis, hypercoagulability,

inflammation and endothelial dysfunction.

- The tolerability of NAC

- The frequency of use of pain medication at home

- The frequency of SCD complications (e.g. stroke)

- Time in days to first painful crisis and first hospital admission

# Study description

### Background summary

Pain is an invalidating hallmark of Sickle Cell Disease (SCD) and has a considerable impact on the Quality of Life (QoL) of patients and the medical health care system. Oxidative stress is hypothesized to play a central role in its pathophysiology. This is supported by the fact that markers of oxidative stress are associated with the extent of chronic organ damage and pain. In an

open label randomized pilot study we demonstrated that administration of a scavenger of free oxygen radicals (oral N-Acetylcysteine; NAC) during 6 weeks reduced markers of oxidative stress. In another pilot study a profound effect of NAC on the hospitalization rate for painful crises was demonstrated. Our hypothesis is that NAC is able to reduce the incidence of daily life pain in patients with SCD

**Study objective**

In this study the effect of the administration of NAC on the frequency and severity of pain and painful crises in daily life will be assessed as well as the related frequency and length of hospital admissions and health related quality of life. In addition, several biomarkers will be monitored and societal costs will be evaluated.

**Study design**

SCD patients are treated with either NAC or placebo in a multicenter, randomized, controlled double blind trial for a period of 6 months. A run-in period of 2 weeks will be take place before randomization to evaluate compliance concerning the completion of a pain diary. Patients with insufficient compliance will not be randomised for further study participation. Total duration of this trial including follow-up will be 6.5 months. Patients are treated with either twice daily 1 tablet of 600mg NAC orally or 1 tablet placebo twice daily.

**Intervention**

N-acetylcystein 600mg twice a day or placebo twice a day

**Study burden and risks**

The risks of participation in this study are predicted to be negligible. NAC is a drug that has been registered for years for other indications and has been studied in a wide age range, in large patient cohorts with different dosages. It has proven to be safe and have only infrequent, limited side effects (occasionally nausea, vomiting or urticaria).
Patients will have to take study medication twice daily. Furthermore, participants will undergo blood sampling more frequently than normally; Every 3 months, in total 3 times, instead of 1-2 times with regular follow-up. They will be seen monthly in outpatient department to monitor outcomes instead of once every 6 months. Also, subjects will have to fill out a daily pain diary for a total of 6.5 months and will be asked to fill out three questionnaires at 0, 3 and 6 months after the start of intervention.

Potential benefit of this study is that NAC may be able to reduce the frequency

and/or severity of pain and painful crises and related hospital admission by reducing oxidative stress. If we are able to find evidence for our hypothesis, the use of NAC in SCD patients may lead to fewer pain complaints, with a potential improvement in QoL, and a potential decrease in pain related healthcare consumption and its costs worldwide.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

- Age 12 years or older
- Either HbSS, HbSC, HbS*0- or HbS*+-thalassemia genotype
- History of at least 1.0 painful crisis per year in the past 3 years (hospital admission is not

obligatory here).
- Written informed consent from patient/parent/guardian

### Exclusion criteria

- Chronic blood transfusion or transfusion in the preceding 3 months
- Painful crisis in the last 4 weeks (hospital admission is not obligatory here)
- Pregnancy, breastfeeding or the desire to get pregnant in the following 9 months
- Known active gastric/duodenal ulcers
- Hydroxycarbamide (HC) treatment with unstable dose in the last 3 months or started on HC shorter then 6 months prior to study.
- Known poor compliance in earlier trials regarding the completion of pain diaries.
- Insufficient compliance in run-in period.
- - Known of hypersensitivity to acetylcysteine or one of the other components of the study medication
-Use of pain medication for sickle-cell related pains on more than 15 days per month in the past 6 months (*chronic pain*).

## Study design

### Design

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

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 03-04-2013 |
| Enrollment: | 65 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | N-acetylcystein |
| Generic name: | acetylcystein |
| Registration: | Yes - NL outside intended use |

## Ethics review

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| Approved WMO Date: | 28-01-2013 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-03-2013 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 22-04-2014 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 08-06-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-02-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 09-02-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# 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 | EUCTR2012-004892-37-NL |
| CCMO | NL41205.018.12 |