

# LIMIT-1: Lowering the Incidence of vascular complications with Metformin in patients with Impaired glucose tolerance and a recent TIA or minor ischemic stroke: a phase 2, randomized, controlled trial

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Metformin will be tolerated in patients with TIA or minor ischemic stroke and will result in blood glucose lowering.

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

## Samenvatting

### ID

NL-OMON26223

### Bron

Nationaal Trial Register

### Verkorte titel

LIMIT-1

### Aandoening

glucose intolerance  
metformin  
TIA  
stroke, ischemic  
trial

### Ondersteuning

**Primaire sponsor:** S.E. Vermeer, MD, PhD

**Overige ondersteuning:** No funding parties

## Onderzoeksproduct en/of interventie

### Uitkomstmaten

#### Primaire uitkomstmaten

1. Tolerability of metformin treatment (measured as number of patients still on treatment after 3 months);
2. The safety of metformin treatment (which will be continuously monitored)
3. The adjusted difference in 2-hour post-load glucose levels at 3 months.

## Toelichting onderzoek

### Achtergrond van het onderzoek

#### Abstract

Background Impaired glucose tolerance, an intermediate metabolic state between normal glucose tolerance and diabetes mellitus defined by 2-hour post-load glucose levels of 7.8-11.0 mmol/L, is associated with an increased risk of stroke in patients with cardiovascular disease. Intensive glucose control with oral antidiabetic drugs have been shown to reduce the diabetes incidence in patients with impaired glucose tolerance without cardiovascular disease. Whether pharmacotherapeutical intervention reduce the risk of cardiovascular events in patients with TIA or minor ischemic stroke and impaired glucose tolerance is unknown.

Aim To examine the safety, tolerability, and effect on glucose metabolism of metformin treatment in non-diabetic patients with TIA or minor ischemic stroke and impaired glucose tolerance.

Design This is a phase 2, randomized, controlled, open-label trial with blind outcome assessment among 40 non-diabetic patients with impaired glucose tolerance who recently had a TIA or minor ischemic stroke. Patients will be randomized for metformin or no oral antidiabetic drug on top of optimal standard treatment including lifestyle advice. The primary outcomes will be the safety, and tolerability of metformin treatment and the adjusted difference in 2-hour post-load glucose levels at 3 months between treatment groups. Secondary outcomes will be the difference in fasting glucose levels, insulin resistance, body mass index, and percentage of patients with a normal glucose tolerance. All analyses will be done according to the intention-to-treat principle.

### Doel van het onderzoek

Metformin will be tolerated in patients with TIA or minor ischemic stroke and will result in blood glucose lowering.

## Onderzoeksproduct en/of interventie

Patients will be randomized for metformin or no oral antidiabetic drug (open-label) on top of optimal standard treatment, including lifestyle advice aimed at weight reduction and regular physical exercise. Patients allocated to metformin will be treated with metformin for 3 months from the day of randomization until study end. They will start with a daily dose of 500 mg that will be slowly increased in one-month time to a daily dose of 2,000 mg in two gifts. All patients will be followed for 3 months.

## Contactpersonen

### Publiek

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### Wetenschappelijk

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## Deelname eisen

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

1. Men or women 18 years and over;
2. TIA/minor ischemic stroke (modified Rankin Score 3 or less) within 6 months;
3. Impaired fasting glucose (fasting glucose level of 5.6 to 6.9 mmol/L) and/or impaired

glucose tolerance (2-hour post-load glucose level of 7.8 to 11.0 mmol/L);

4. Informed consent

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

1. Known or newly diagnosed diabetes mellitus;
2. Contraindication for metformin:
  - a. renal impairment (serum creatinine >135 micromol/L for men, and >110 micromol/L for women),
  - b. hepatic disease (liver enzymes increased twice the upper limit of normal), c. a past history of lactic acidosis,
  - d. cardiac failure requiring pharmacological therapy,
  - e. chronic hypoxic lung disease,
  - f. pregnancy,
  - g. breast feeding;
3. Severe comorbidity interfering with follow-up

## **Onderzoeksopzet**

### **Opzet**

|                  |                       |
|------------------|-----------------------|
| Type:            | Interventie onderzoek |
| Onderzoeksmodel: | Parallel              |
| Blindering:      | Enkelblind            |
| Controle:        | N.v.t. / onbekend     |

### **Deelname**

|                         |                      |
|-------------------------|----------------------|
| Nederland               |                      |
| Status:                 | Werving gestart      |
| (Verwachte) startdatum: | 01-02-2007           |
| Aantal proefpersonen:   | 40                   |
| Type:                   | Verwachte startdatum |

## **Ethische beoordeling**

Positief advies

Datum: 09-03-2007  
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        | NL905          |
| NTR-old        | NTR929         |
| Ander register | :              |
| ISRCTN         | ISRCTN54960762 |

## Resultaten