# LIMIT: 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

Published: 13-11-2006
Last updated: 14-05-2024

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.

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Glucose metabolism disorders (incl diabetes mellitus) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON30741

**Source**
ToetsingOnline

**Brief title**
LIMIT phase 2

### Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Central nervous system vascular disorders

**Synonym**
impaired glucose tolerance, prediabetes

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** glucose intolerance, metformin, secondary prevention trial, TIA

## Outcome measures

### Primary outcome

The primary outcomes of this phase 2 trial 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 outcome

Secondary outcomes will be the difference in fasting glucose levels, insulin resistance, body mass index, and percentage of patients with a normal glucose tolerance after 3 months.

# Study description

### Background summary

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.

### Study objective

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.

### Study 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.

### Intervention

Patients will be randomized for metformin (up to a maximum of 2,000mg/day) or no oral antidiabetic drug on top of optimal standard treatment including lifestyle advice.

### Study burden and risks

Patients will be followed for 3 months, in which they will be examined by a neurologist twice and will undergo a vena puncture twice (2 times including oral glucose tolerance test). Furthermore, half of the patients will be on metformin treatment during 3 months (2 tablets metformin a day). Up to 20% of the patients can experience mainly mild, gastrointestinal side effects at the beginning of metformin treatment, which can be minimized by slow introduction of the drug.

## Contacts

**Public**
Erasmus MC, Universitair Medisch Centrum Rotterdam

Postbus 2040
3000 CA Rotterdam
NL
**Scientific**
Erasmus MC, Universitair Medisch Centrum Rotterdam

Postbus 2040
3000 CA Rotterdam
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

-Age > 18 years
-TIA/minor ischemic stroke < 6 months
-Non-diabetics with impaired glucose tolerance (2hr post-load glucose 7.8-11.0 mmol/L) or impaired fasting glucose (fasting glucose 5.6-6.9 mmol/L)

### Exclusion criteria

-Diabetes mellitus
-Dependency of others (mRankin >= 4)
-Contraindication metformin (severe renal failure, severe hepatic insufficiency, severe heart failure, severe hypoxic lung disease, lactic acidosis in history)
-Severe comorbidity interfering with follow-up

## Study design

### Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Prevention

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 13-12-2006 |
| Enrollment: | 40 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | glucophage |
| Generic name: | metformin |
| Registration: | Yes - NL outside intended use |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 13-11-2006 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 05-12-2006 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# 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 | EUCTR2006-005772-41-NL |
| ISRCTN | ISRCTN54960762 |
| CCMO | NL15011.078.06 |