# Effect of additional treatment with EXenatide in patients with an Acute Myocardial Infarction: the EXAMI trial

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The primary objective is to determine whether additional treatment with exenatide in patients with acute myocardial infarction and treated with primary PCI, leads to a more preserved left ventricular function, compared to placebo in addition to...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Heart failures |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON40038

**Source**
ToetsingOnline

**Brief title**
EXAMI

### Condition

- Heart failures

**Synonym**
Acute myocardial infarction

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** acute myocardial infarction, exenatide, primary percutaneous coronary intervention, reperfusion injury

## Outcome measures

### Primary outcome

Infarct size measured as the final infarct size on Delayed Enhancement (DE) MRI

at 4 months as a percentage of the area at risk on T2 weighed MRI at 3-7 days.

### Secondary outcome

The difference between all treatment groups in:

-Myocardial infarct size as measured by serum CKmb release during the first 72

hours after PCI.

-Regional myocardial function based on a MRI segmental analysis at 3-7 days

and at 4 months.

-Global left ventricular ejection fraction, Left Ventricular End Systolic

Volume (LVESV), Left Ventricular End Diastolic Volume (LVEDV) at 3-7 days and

at 4 months measured by MRI.

-Presence and extent of microvascular obstruction measured by DE MRI 3-7 days

after PCI.

-Global left ventricular ejection fraction, LVESV, LVEDV at 2-7 days and at 4

months measured by Echocardiography.

-Global left ventricular ejection fraction measured by strain echocardiography.

-The occurrence within 4 months of a Major Adverse Cardiac Event (MACE)

defined as cardiac death, myocardial infarction, coronary bypass grafting, or a

repeat PCI .

-Repeat PCI in the infarct related artery during 4 months follow up.

-Serum-glucose levels during the first 72 hours.

-Side effects of exenatide

-Angiographic parameters as Trombolysis In Myocardial Infarction (TIMI) frame

count and TIMI blush grade after PCI

-SPECT data after PCI. Comparison with MRI perfusion defects

-Resistance measurements by ComboWire

# Study description

**Background summary**

Myocardial infarction causes loss of myocytes and may lead to loss of ventricular function, morbidity and mortality. It is well known that preservation of myocytes during myocardial infarction will affect the infarct size and prognosis. The most effective therapy is early reperfusion of the ischemic myocardium by percutaneous coronary intervention (PCI). Reperfusion limits myocardial ischemic necrosis, however, it also results in accelerated apoptosis due to calcium overload, inflammation and oxidative stress; a phenomenon referred to as reperfusion injury. Therefore, large myocardial infarctions still occur despite adequate reperfusion therapy. Glucagon-like peptide (GLP)-1 is a gut incretin hormone, which is released by the gut in response to nutrient intake. It facilitates glucose induced insulin release, and therefore, analogues of GLP-1 are now being used for the treatment of diabetes. Furthermore, GLP-1 has been demonstrated to possess anti-apoptotic properties that may protect the heart against ischaemia - reperfusion injury. Multiple in vitro and in vivo animal studies showed evidence for this hypothesis. So far only one study tested GLP-1 infusion during acute myocardial infarction in human patients and showed improvement of left ventricular function when using GLP-1 infusion in addition to primary PCI alone. Another recent clinical study (2011) demonstrated that additional treatment with the GLP-1 receptor agonist exenetide in patient with an acute myocardial infarction undergoing PCI improves mycardial salvage. Because it concerns only one study, more research is required to confirm the results. In this randomized study we will assess the additional effect of exenatide on left ventricular function after acute myocardial infarction treated with primary percutaneous coronary intervention (PCI) compared to placebo. Magnetic Resonance Imaging (MRI) will be used to asses left ventricular function during admission and at 4 months

follow up.

### Study objective

The primary objective is to determine whether additional treatment with exenatide in patients with acute myocardial infarction and treated with primary PCI, leads to a more preserved left ventricular function, compared to placebo in addition to primary PCI.

### Study design

A prospective randomized placebo controlled two-arm study.
After informed consent has been obtained patients are randomized to the following 2 groups: (1) PCI and placebo (2) PCI and exenatide infusion started before PCI and continued for 72 hours after PCI. ComboWire measurements will be performed in all patients after PCI. SPECT will be performed in all patients after PCI. MRI measurements are performed in all patiens 3 to 7 days after PCI and at 4 months. Echocardiography is performed in all patients 2-7 days after PCI and at 4 months. Close glucose control is performed from hospital admission until discharge and if indicated also after discharge.

### Intervention

Administration of exenatide (exenatide group) or placebo (placebogroup) in addition to standard treatment of acute myocardial infarction by PCI.

### Study burden and risks

-during exenatide treatment there is a small risk of developing hypoglycaemia. Therefore bloodglucose levels will be strictly monitored.
-during exenatide treatment patients might suffer from side effects like nausea.
-during admission and at 4 months follow up echocardiography and CMR will be performed.
Small radiation dose with 1 SPECT investigations ± 3,5 mSv

## Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

-First myocardial infarction
-ST elevation of at least 0,1mV in at least 2 contiguous leads
- > 18 years of age
- Delay between onset of sustained chestpain and PCI < 6 hours

## Exclusion criteria

-Diabetes type I or II
-Heartfailure (Kilip III or IV)
-No definite Culprit
-More than one occluded vessel, or a more than 70% stenosis by visual assessment in a non-culprit vessel.
-No recanalisation achieved of the occluded coronary artery
-Decreased renal function eGFR < 30ml/min
-Any contraindication for MRI
- TIMI 2 or 3 flow in culprit lesion at presentation

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| 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): | 01-11-2009 |
| Enrollment: | 125 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Byetta |
| Generic name: | Exenatide |
| Registration: | Yes - NL outside intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 07-08-2009 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 03-11-2009 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

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|---|---|
| Approved WMO Date: | 25-01-2010 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 10-09-2012 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 16-04-2013 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 12-09-2013 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 17-03-2014 |
| 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 | EUCTR2009-014272-21-NL |

| Register | ID |
| --- | --- |
| CCMO | NL28593.029.09 |