# GLP-1 for bridging of hyperglycaemia during cardiac surgery: a randomized controlled trial

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

## Summary

### ID

NL-OMON45357

**Source**
ToetsingOnline

**Brief title**
The GLOBE trial

### Condition

- Glucose metabolism disorders (incl diabetes mellitus)

**Synonym**
high blood glucose concentration

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W,Novo Nordisk

## Intervention

**Keyword:** Cardiac Surgery, GLP-1, Hyperglycaemia, Insulin

## Outcome measures

### Primary outcome

The main study endpoint is reduction in the number of patients needing

perioperative insulin treatment when aiming for plasma glucose < 8 mmol l-1.

### Secondary outcome

We will assess the following secondary outcome parameters:

* Total perioperative insulin use (IU/day)

* Number of insulin administrations

* Composite postoperative complications*

* Glucose control in the perioperative period, as assessed by the mean

perioperative glucose

* Number of perioperative hyperglycaemic events (>11 mmol l-1)

* Number of moderate perioperative hypoglycaemic events (<4 mmol l-1)

* Number of severe perioperative hypoglycaemic events (<2.3 mmol l-1)

* Percentage of time spent in target range (%TIR) for CGM measurements

* Proportion of patients with postoperative nausea and vomiting

# Study description

### Background summary

Hyperglycemie ontwikkelt zich in de meerderheid van patiënten die cardiale chirurgie ondergaan. Er is een duidelijke associatie tussen hyperglycemie en postoperatieve complicaties. De implementatie van perioperatieve insuline behandeling wordt gehinderd door het risico op hypoglycemie. Glucagon Like

Peptide 1 (GLP-1) behandeling is een veelbelovende therapie voor perioperatieve hyperglycemie tijdens cardiale chirurgie. Het heeft het potentieel om glucose te verlagen en de nood aan insuline te verminderen. Zodoende kan het, het risico op iatrogene hypoglycemie verkleinen.

## Study objective

We hypothesize that liraglutide treatment (a GLP-1 analogue), initiated before cardiac surgery, is effective in lowering the number of patients needing perioperative insulin adjustments and reducing the total amount of insulin needed in the perioperative period when aiming for a moderate glucose target of < 8 mmol l-1.

## Study design

We will perform a randomized double blind placebo controlled trial in 5 Dutch cardiac surgery centres.

## Intervention

Patients will be randomized (1:1) to perioperative liraglutide treatment or placebo. Liraglutide or placebo 0.6 mg subcutaneously (sc) the day before surgery and 1.2 mg sc on the day of surgery will be administered. In both arms the glucose target range is <8 mmol l-1.

## Study burden and risks

For study purposes, an additional 18.4 ml of blood will be drawn. This will be taken from intravenous or intra-arterial catheters that have been inserted for clinical purposes. Common adverse events with liraglutide treatment are related to the gastrointestinal system, nausea and diarrhoea as reported most frequently. In addition, there is a small risk of hypoglycaemia, which is minimized by frequent glucose monitoring. All adverse events are mostly mild and the drop-out rate from clinical trials due to adverse events has been low. Patient might benefit from this intervention by improved perioperative glucose control without insulin. This reduces hypoglycaemia risk and might reduce other postoperative complications. In general this study will provide more insight in the effect of liraglutide as a glucose-lowering agent to prevent insulin use in the perioperative setting.
Before the first study drug treatment the sensor of a subcutaneous continuous glucose monitor is inserted into the subcutaneous tissue. This will be done in a subset of 26 patients (see sample size calculation) included in the AMC or OLVG (for logistical reasons).

# 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

* Adult patients, aged 18-80 years (inclusive),
* No known diabetes mellitus, or
* Known diabetes mellitus type 2 on oral glucose lowering medication, diet or total daily insulin dose *0.5 IU/kg
* Scheduled for an elective cardiac surgical procedure.
* Informed consent obtained before any trial-related activities are carried out.

## Exclusion criteria

* Diabetes mellitus type 1
* Emergency surgery

* Receiving oral corticosteroid therapy
* History of pancreatic surgery or acute or chronic pancreatitis
* Personal or family history of medullary thyroid cancer (MTC) or Multiple Endocrine Neoplasia syndrome type 2 (MEN2)
* Heart failure NYHA class IV
* Serum-creatinine * 133 *mol l-1 for males and * 115 *mol l-1 for females
* Female of child-bearing potential who is pregnant, breast-feeding or intend to become pregnant or is not using adequate contraceptive methods
* Current treatment with GLP-1 analogues
* Known or suspected allergy to trial products or other drugs in the same class

# Study design

## Design

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| Study phase: | 4 |
| 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): | 09-06-2017 |
| Enrollment: | 274 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Victoza |
| Generic name: | Liraglutide |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 30-01-2017 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-04-2017 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 06-11-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 07-11-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-11-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 29-01-2018 |
| 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 | EUCTR2017-000043-40-NL |
| CCMO | NL60461.018.17 |
| Other | Reeds ingediend bij NTR, registratie nog niet afgerond. |