# Clinical trial results:
# Perioperative intravenous insulin, GIK or GLP-1 treatment in DM

## Summary

| | |
|---|---|
| EudraCT number | 2012-005291-34 |
| Trial protocol | NL |
| Global end of trial date | 20 February 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 May 2021 |
| First version publication date | 06 May 2021 |
| Summary attachment (see zip file) | publication (Polderman_et_al-2017-Anaesthesia.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | NL41467 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Amsterdam UMC |
| Sponsor organisation address | Meibergdreef 9, Amsterdam, Netherlands, |
| Public contact | J.A.W. Polderman, AMC, Amsterdam, J.A.Polderman@amc.uva.nl |
| Scientific contact | J.A.W. Polderman, AMC, Amsterdam, J.A.Polderman@amc.uva.nl |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 29 September 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 February 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 February 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the optimal treatment strategy for diabetes mellitus during non-cardiac surgery

Protection of trial subjects:

All trial subjects were followed until 30 days after surgery.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 June 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Netherlands: 167 |
| Worldwide total number of subjects | 167 |
| EEA total number of subjects | 167 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 93 |
| From 65 to 84 years | 74 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patients were recuited on the pre-assessment visit

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 167 |
| Number of subjects completed | 167 |

### Period 1

| | |
|---|---|
| Period 1 title | Recruitment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

not blinded

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | GIK infusion |

Arm description:

patients receiving a GIK infusion perioperatively

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | novorapid |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

novorapid was added to glucose 5% solution for intravenous drip

| | |
|---|---|
| Investigational medicinal product name | potassium |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

1 ampule of potassium was added to glucose 5% solution for infusion

| | |
|---|---|
| **Arm title** | Bolus |

Arm description:

received insulin boluses

| | |
|---|---|
| Arm type | Active comparator |

| | |
|---|---|
| Investigational medicinal product name | novorapid |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Intravenous drip use |

Dosage and administration details:
novorapid was added to glucose 5% solution for intravenous drip

| | |
|---|---|
| **Arm title** | liraglutide |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | liraglutide |
| Investigational medicinal product code | |
| Other name | victoza |
| Pharmaceutical forms | Solution for injection/infusion in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:
Liraglutide 0,6 en 1,2 mg

| **Number of subjects in period 1** | GIK infusion | Bolus | liraglutide |
|---|---|---|---|
| Started | 59 | 55 | 53 |
| Completed | 53 | 53 | 44 |
| Not completed | 6 | 2 | 9 |
| Protocol deviation | 6 | 2 | 9 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | GIK infusion |
| Reporting group description: patients receiving a GIK infusion perioperatively | |
| Reporting group title | Bolus |
| Reporting group description: received insulin boluses | |
| Reporting group title | liraglutide |
| Reporting group description: - | |

| Reporting group values | GIK infusion | Bolus | liraglutide |
|---|---|---|---|
| Number of subjects | 59 | 55 | 53 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 28 | 32 | 25 |
| From 65-84 years | 31 | 23 | 28 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 62 | 61 | 62 |
| standard deviation | ± 8.1 | ± 8.6 | ± 8.8 |
| Gender categorical | | | |
| gender | | | |
| Units: Subjects | | | |
| Female | 29 | 27 | 28 |
| Male | 30 | 28 | 25 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 167 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 85 | | |

| | | | |
|---|---|---|---|
| From 65-84 years | 82 | | |
| 85 years and over | 0 | | |

| | | | |
|---|---|---|---|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| gender | | | |
| Units: Subjects | | | |
| Female | 84 | | |
| Male | 83 | | |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | GIK infusion |
| Reporting group description:<br>patients receiving a GIK infusion perioperatively | |
| Reporting group title | Bolus |
| Reporting group description:<br>received insulin boluses | |
| Reporting group title | liraglutide |
| Reporting group description: - | |

| Primary: glucose 1 hour postoperative | |
|---|---|
| End point title | glucose 1 hour postoperative |
| End point description:<br>glucose 1 hour postoperative | |
| End point type | Primary |
| End point timeframe:<br>glucose 1 hour postoperative | |

| End point values | GIK infusion | Bolus | liraglutide | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 53 | 53 | 44 | |
| Units: mmol/l | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| primary endpoint | 7.5 (6.4 to 8.3) | 7.6 (6.4 to 8.9) | 6.6 (5.6 to 7.7) | |

### Statistical analyses

| Statistical analysis title | Mann Withney U |
|---|---|
| Comparison groups | GIK infusion v Bolus v liraglutide |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (final values) |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.05 |
| upper limit | 0.05 |

| Variability estimate | Standard deviation |
|---|---|

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: until 30 days postoperatively | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24 |

| Reporting groups | |
|---|---|
| Reporting group title | GIK infusion |
| Reporting group description: patients receiving a GIK infusion perioperatively | |
| Reporting group title | Bolus |
| Reporting group description: received insulin boluses | |
| Reporting group title | liraglutide |

Reporting group description: -

| Serious adverse events | GIK infusion | Bolus | liraglutide |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 53 (11.32%) | 5 / 53 (9.43%) | 2 / 49 (4.08%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Embolism | Additional description: lung embolism or bleeding | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 53 (5.66%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Infection | Additional description: wound infection or sepsis | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 2 / 53 (3.77%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 1 %

| **Non-serious adverse events** | GIK infusion | Bolus | liraglutide |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 1 / 53 (1.89%) | 1 / 49 (2.04%) |
| Endocrine disorders | | | |
| hypoglycemia | Additional description: mild hypoglycemia under 4.0 mmol per liter | | |
| alternative dictionary used: MedDRA 24 | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 1 / 53 (1.89%) | 1 / 49 (2.04%) |
| occurrences (all) | 4 | 1 | 1 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported