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 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 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 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: patients receiving a GIK infusion perioperatively	
Reporting group title	Bolus
Reporting group description: 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: glucose 1 hour postoperative	
End point type	Primary
End point timeframe: 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