Clinical trial results:
Assessment of Hepatic Glucose Production Following Repeated Glucagon Administration in Type 1 Diabetes Patients

Summary

EudraCT number	2013-001407-36
Trial protocol	AT
Global end of trial date	10 April 2014

Results information

Result version number	v1 (current)
This version publication date	26 March 2021
First version publication date	26 March 2021

Trial information

Trial identification

Sponsor protocol code	HEPPI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Graz
Sponsor organisation address	Auenbruggerplatz 15, Graz, Austria, A-8036
Public contact	Center for Medical Research (ZMF), Medical University of Graz; Dept. of Internal Medicine; Division of Endocrinology and Diabetology, +43 31638572831, werner.regittnig@medunigraz.at
Scientific contact	Center for Medical Research (ZMF), Medical University of Graz; Dept. of Internal Medicine; Division of Endocrinology and Diabetology, +43 31638572831, werner.regittnig@medunigraz.at

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	31 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2014
Global end of trial reached?	Yes
Global end of trial date	10 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of repeated subcutaneous glucagon administration on the hepatic glucose production in type 1 diabetic patients under fed and fasted conditions.

Protection of trial subjects:

Number of intravenous catheters inserted as well as the number of blood samples drawn during the two study visits were minimised to minimise distress and pain.

Background therapy:

On the days before and after the two study visits, study subjects were either treated with multiple daily injections (MDI) of insulin or continuous subcutaneous insulin infusion (CSII).

Evidence for comparator: -

Actual start date of recruitment	06 May 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	9
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the diabetes out-patient clinic of the Medical University of Graz. Recruitment period lasted from May 2013 to April 2014.

Pre-assignment

Screening details:

10 subjects were screened. They were of both sexes, in the age group of 18–64 years and diagnosed with type 1 diabetes. They had to have HbA1C values of <10%, and had to be treated with multiple daily injection of insulin or continuous subcutaneous insulin infusion. One patient was excluded due to a screening failure.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Fasted Conditions

Arm description:

In this arm, subjects were given three subcutaneous boluses of glucagon (1 mg) in the fasted state (i.e., 20 hours post-meal). The boluses of glucagon were separated by 180 minutes. To restore normoglycemia after each glucagon bolus, the subjects engaged in moderate-intensity exercise.

Arm type	crossover
Investigational medicinal product name	Glucagon
Investigational medicinal product code	SUB02347MIG
Other name	GlucaGen
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 x 1 mg

Arm title	Fed Conditions

Arm description:

In this arm, subjects were given three subcutaneous boluses of glucagon (1 mg) in the fed state (i.e., 6 hours post-meal). The boluses of glucagon were separated by 180 minutes. To restore normoglycemia after each glucagon bolus, the subjects engaged in moderate-intensity exercise.

Arm type	crossover
Investigational medicinal product name	Glucagon
Investigational medicinal product code	SUB02347MIG
Other name	GlucaGen
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 x 1 mg

Number of subjects in period 1	Fasted Conditions	Fed Conditions
Started	7	6
Completed	4	4
Not completed	3	2
Adverse event, non-fatal	2	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period
Reporting group description:	
Overall Population as this is a cross-over trial	

Reporting group values	Overall Period	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	9	9	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	36.7		
standard deviation	± 7.8	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	6	6	

End points

End points reporting groups

Reporting group title	Fasted Conditions

Reporting group description:

In this arm, subjects were given three subcutaneous boluses of glucagon (1 mg) in the fasted state (i.e., 20 hours post-meal). The boluses of glucagon were separated by 180 minutes. To restore normoglycemia after each glucagon bolus, the subjects engaged in moderate-intensity exercise.

Reporting group title	Fed Conditions

Reporting group description:

In this arm, subjects were given three subcutaneous boluses of glucagon (1 mg) in the fed state (i.e., 6 hours post-meal). The boluses of glucagon were separated by 180 minutes. To restore normoglycemia after each glucagon bolus, the subjects engaged in moderate-intensity exercise.

Primary: AUC HGP - fasted vs. fed conditions

End point title	AUC HGP - fasted vs. fed conditions

End point description:

End point type	Primary

End point timeframe:

Area under the hepatic glucose production curve (AUC HGP) from 0 to 90 minutes after the glucagon bolus injections.

End point values	Fasted Conditions	Fed Conditions		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: mg/kg				
arithmetic mean (standard error)	1224.9 (± 118.2)	1268.4 (± 79.0)		

Statistical analyses

Statistical analysis title	AUC HGP - fasted vs. fed conditions
Comparison groups	Fasted Conditions v Fed Conditions
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.82
Method	2-sided paired t-test

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from the onset of screening to the last patient last visit	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
Loss of consciousness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	6 / 9 (66.67%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		

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