Clinical trial results:
Treat-To-Target Trial of Continuous Subcutaneous , sensor-augmented insulin-pump therapy in new-onset diabetes after transplantation (SAPT-NODAT): Efficacy and Safety of an Intensive Insulin Protocol in Renal Transplant Recipients Receiving a Tacrolimus-based Immunosuppression

Summary

EudraCT number	2012-000216-28
Trial protocol	AT
Global end of trial date	22 May 2018

Results information

Result version number	v1 (current)
This version publication date	01 July 2021
First version publication date	01 July 2021

Trial information

Trial identification

Sponsor protocol code	KIMIII

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Staff Physician, Med. Univ. Wien, UK für Innere III, manfred.hecking@meduniwien.ac.at
Scientific contact	Staff Physician, Med. Univ. Wien, UK für Innere III, manfred.hecking@meduniwien.ac.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	06 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate superiority of continuous subcutaneous sensor-augmented insulin-pump therapy (SAPT) with an insulin pump from Medtronic (Paradigm® Velo) for a period of approximately 3 months post-transplantation, and aiming for a pre-supper target capillary blood glucose level of 110 mg/dL against post-transplant hyperglycemia, in comparison to conventional treatment, and as evaluated by HbA1c at 3 months post-transplantation (comparison will be made against the simultaneously monitored control group of the ITP-NODAT study [=arm B])

Protection of trial subjects:

regularly blood sugar control, glycemic profiles, monitoring of adverse events at regularly visits

Background therapy:

standard of care therapy

Evidence for comparator: -

Actual start date of recruitment	07 April 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: 85
Worldwide total number of subjects	85
EEA total number of subjects	85

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)	69
From 65 to 84 years	16

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All non-diabetic patients who were scheduled for transplantation (both deceased and living donors) were informed and invited to participate in either ITP-NODAT or SAPT-NODAT. Patients were randomized for participation in either SAPT-NODAT or ITP-NODAT.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	85
Number of subjects completed	85

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	basal insulin treatment

Arm description:

patients who received basal insulin

Arm type	Active comparator
Investigational medicinal product name	insulin isophane Humulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

according to pre- specified protocol, starting point: blood glucose > 140 mg /dl at pre-supper measurement

Arm title	control group

Arm description:

standard of care for hyperglycemia (sliding scale for short acting insulin as pre-specified in the protocol) - no product has been specified

Arm type	standard of care for hyperglycemia (sliding scale

No investigational medicinal product assigned in this arm

Arm title	Insulin Pump

Arm description:

MiniMed Paradigm Veo Insulin Pump with the Sure-T

Arm type	Experimental
Investigational medicinal product name	MiniMed Paradigm Veo Insulin Pump with the Sure-T
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Subcutaneous use

Dosage and administration details:

MiniMed Paradigm Veo Insulin Pump with the Sure-T was implanted to administer short acting insulin according to pre-specified protocol

Number of subjects in period 1	basal insulin treatment	control group	Insulin Pump
Started	26	31	28
Completed	19	27	23
Not completed	7	4	5
Consent withdrawn by subject	3	2	2
exitus	1	-	-
Post-operative complications	1	-	2
Lost to follow-up	-	2	-
nephrectomy	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	basal insulin treatment
Reporting group description:	
patients who received basal insulin	
Reporting group title	control group
Reporting group description:	
standard of care for hyperglycemia (sliding scale for short acting insulin as pre-specified in the protocol) - no product has been specified	
Reporting group title	Insulin Pump
Reporting group description:	
MiniMed Paradigm Veo Insulin Pump with the Sure-T	

Reporting group values	basal insulin treatment	control group	Insulin Pump
Number of subjects	26	31	28
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)	20	25	24
From 65-84 years	6	6	4
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	13	4
Male	17	18	24

Reporting group values	Total		
Number of subjects	85		
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)	69		
From 65-84 years	16		
85 years and over	0		

Gender categorical Units: Subjects			
Female	26		
Male	59		

End points

End points reporting groups

Reporting group title	basal insulin treatment
Reporting group description:	
patients who received basal insulin	
Reporting group title	control group
Reporting group description:	
standard of care for hyperglycemia (sliding scale for short acting insulin as pre-specified in the protocol) - no product has been specified	
Reporting group title	Insulin Pump
Reporting group description:	
MiniMed Paradigm Veo Insulin Pump with the Sure-T	

Primary: HbA1c

End point title	HbA1c
End point description:	
End point type	Primary
End point timeframe:	
HbA1c at 3 months	

End point values	basal insulin treatment	control group	Insulin Pump	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	27	23	
Units: percent				
median (inter-quartile range (Q1-Q3))	5.3 (4.7 to 5.6)	5.0 (4.7 to 6.3)	5.6 (5.4 to 6.1)	

Statistical analyses

Statistical analysis title	Mann-Whitney-U test
Comparison groups	control group v Insulin Pump v basal insulin treatment
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Confidence interval	
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2 years	
Adverse event reporting additional description: Enrollment until end of follow up	
Assessment type	Systematic

Dictionary used	
Dictionary name	no dictionary used
Dictionary version	n.a.

Reporting groups	
Reporting group title	basal insulin treatment
Reporting group description: patients who received basal insulin	
Reporting group title	control group
Reporting group description: standard of care for hyperglycemia (sliding scale for short acting insulin as pre-specified in the protocol) - no product has been specified	
Reporting group title	Insulin Pump
Reporting group description: MiniMed Paradigm Veo Insulin Pump with the Sure-T	

Serious adverse events	basal insulin treatment	control group	Insulin Pump
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 26 (7.69%)	1 / 31 (3.23%)	2 / 28 (7.14%)
number of deaths (all causes)	2	1	2
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Hypoglycaemia			
alternative dictionary used: MedDRA 23.0			
subjects affected / exposed	2 / 26 (7.69%)	1 / 31 (3.23%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 2

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

Non-serious adverse events	basal insulin treatment	control group	Insulin Pump
Total subjects affected by non-serious adverse events subjects affected / exposed	24 / 26 (92.31%)	28 / 31 (90.32%)	24 / 28 (85.71%)
Investigations Other Adverse Events subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	4 / 31 (12.90%) 4	6 / 28 (21.43%) 6
Injury, poisoning and procedural complications Injury, procedural complications subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	2 / 31 (6.45%) 2	2 / 28 (7.14%) 2
Surgical and medical procedures Surgical complications subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	1 / 31 (3.23%) 1	1 / 28 (3.57%) 1
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	2 / 31 (6.45%) 2	0 / 28 (0.00%) 0
Hypoglycaemia 41-60mg/dl alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 31 (0.00%) 0	2 / 28 (7.14%) 2
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 31 (6.45%) 3	1 / 28 (3.57%) 1
Renal and urinary disorders Graft loss subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	4 / 31 (12.90%) 4	3 / 28 (10.71%) 3
Rejection subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4	4 / 31 (12.90%) 5	1 / 28 (3.57%) 1
Other kidney disorders			

subjects affected / exposed	4 / 26 (15.38%)	3 / 31 (9.68%)	1 / 28 (3.57%)
occurrences (all)	4	4	1
Infections and infestations			
Infections			
subjects affected / exposed	6 / 26 (23.08%)	6 / 31 (19.35%)	7 / 28 (25.00%)
occurrences (all)	8	9	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 July 2015	This amendment describes the number of the patients who will be recruited by each center. Originally 380 patients should be recruited of the ITP and the SAPT-NODAT study: 150 patients at the University of Michigan Transplant Center (US), 50 patients at the Medical University of Vienna + 25 patients for the SAPT-NODAT arm (A), 40 patients at the University Barcelona (Spain), 60 patients at the Campus Charité Mitte, Berlin (D), 40 patients at the Campus Charité Virchow-Klinikum, Berlin (D) and 40 patients at the Medical University Graz (A). This amendment concerns the number of the patients recruited: The University of Michigan was not able to recruit 150 patients, but recruited 50 patients. Therefore, the Medical University of Vienna should recruit 102 patients (34 patients for the control group, 34 patients for the basal insulin group and 34 patients for the pump therapy group).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported