Clinical trial results:
Assessment of the Hydraulic Tissue Resistance at the Site of Subcutaneous Insulin Infusion in Patients with Type 1 Diabetes

Summary

EudraCT number	2015-005311-32
Trial protocol	AT
Global end of trial date	06 April 2016

Results information

Result version number	v1 (current)
This version publication date	22 November 2021
First version publication date	22 November 2021

Trial information

Trial identification

Sponsor protocol code	RHEO-01

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	22 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 April 2016
Global end of trial reached?	Yes
Global end of trial date	06 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to monitor the tissue hydraulic resistance at the subcutaneous tissue sites of infusion of an insulin and insulin-free solution in patients with type 1 diabetes and to determine the frequency distributions of the tissue hydraulic resistance at these infusion sites over a time period of 7 days.

Protection of trial subjects:

Subjects were individually instructed on the use of the insulin pump employed in the study. Subjects were given written instructions for handling low and high glucose concentrations. Subjects were provided with a 24-hour telephone helpline. Subjects were asked to perform at least seven blood glucose measurements per day and to immediately contact the study team when correction boluses failed to decrease their glucose levels.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 January 2016
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the diabetes out-patient clinics of the Medical University of Graz. Recruitment period lasted from January 2016 to April 2016

Pre-assignment

Screening details:

35 subjects were screened. They were of both sexes, in the age group of 18–65 years and diagnosed with type 1 diabetes. They had to have HbA1C values of <10%, and had to be treated with continuous subcutaneous insulin Infusion (insulin pump therapy). Five subjects were excluded due to screening failures.

Period 1

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

Arms

Arm title	Insulin Infusion Sites

Arm description:

Subjects wore two identical insulin pumps over a period of 7 days. One pump was used for continuous subcutaneous insulin infusion (CSII) therapy and the other for the infusion of an insulin-free solution. At both infusion sites, the tissue flow resistance (TFR) was assessed shortly after establishing the infusion sites (Day 0) and on each of the 7 subsequent days (Days 1-7).

Arm type	experimental, single arm
Investigational medicinal product name	Insulin Aspart
Investigational medicinal product code	SUB08195MIG
Other name	NovoRapid
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

One insulin pump provided insulin aspart to the patient's body at basal and bolus rates. Basal insulin was continuously delivered throughout the day to mimic the background insulin production of the pancreas. Bolus insulin was delivered on demand to match the amount of carbohydrates ingested or to correct high blood glucose. The size of the basal and bolus insulin delivered was dependent on the patient's insulin sensitivity, the current blood glucose value, and total grams of carbohydrates that the patient ingested. The average daily total dose of insulin aspart administered in the study subjects was 45 insulin units.

Number of subjects in period 1	Insulin Infusion Sites
Started	30
Completed	30

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study (overall period)

Reporting group description:

The reporting group data set includes the tissue flow resistances and infusion pressures observed at the insulin infusion sites. As all data sets followed a log-normal distribution, all data are presented as the geometric mean times-divide one geometric standard deviation (geoMean*/geoSD).

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	30	30	
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)	30	30	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	43.5		
standard deviation	± 12.5	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	22	22	

End points

End points reporting groups

Reporting group title	Insulin Infusion Sites

Reporting group description:

Subjects wore two identical insulin pumps over a period of 7 days. One pump was used for continuous subcutaneous insulin infusion (CSII) therapy and the other for the infusion of an insulin-free solution. At both infusion sites, the tissue flow resistance (TFR) was assessed shortly after establishing the infusion sites (Day 0) and on each of the 7 subsequent days (Days 1-7).

Subject analysis set title	Placebo Infusion Sites
Subject analysis set type	Full analysis

Subject analysis set description:

This subject analysis set includes the tissue flow resistances and infusion pressures observed at the placebo infusion sites. As all data sets followed a log-normal distribution, all data are presented as the geometric mean times-divide one geometric standard deviation (geoMean*/geoSD).

Primary: Tissue Flow Resistance on Day 7 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 7 of Infusion Site Use

End point description:

End point type	Primary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on the last study day (Day 7). TFR was computed from the infusion pressure time courses measured on Day 7.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	8.64 (± 3.48)	0.43 (± 6.01)		

Statistical analyses

Statistical analysis title	TFR Day7 - insulin versus placebo infusion sites
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2-sided

Secondary: Tissue Flow Resistance on Day 6 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 6 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 6. TFR was computed from the infusion pressure time courses measured on Day 6.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	7.14 (± 3.38)	0.31 (± 7.89)		

Statistical analyses

Statistical analysis title	TFR Day 6 - insulin versus placebo infusion sites
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.001
Method	paired t-test 2 sided

Notes:

[1] - Analysis was performed using paired t-test on log-transformed data

Secondary: Tissue Flow Resistance on Day 5 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 5 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 5. TFR was computed from the infusion pressure time courses measured on Day 5.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	4.40 (± 6.01)	0.50 (± 6.37)		

Statistical analyses

Statistical analysis title	TFR Day 5 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Tissue Flow Resistance on Day 4 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 4 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 4. TFR was computed from the infusion pressure time courses measured on Day 4.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	4.38 (± 4.12)	0.32 (± 8.26)		

Statistical analyses

Statistical analysis title	TFR Day 4 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Tissue Flow Resistance on Day 3 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 3 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 3. TFR was computed from the infusion pressure time courses measured on Day 3.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	2.48 (± 6.66)	0.29 (± 8.45)		

Statistical analyses

Statistical analysis title	TFR Day 3 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Tissue Flow Resistance on Day 2 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 2 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 2. TFR was computed from the infusion pressure time courses measured on Day 2.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	1.32 (± 5.30)	0.35 (± 7.76)		

Statistical analyses

Statistical analysis title	TFR Day 2 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data.

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Tissue Flow Resistance on Day 1 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 1 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 1. TFR was computed from the infusion pressure time courses measured on Day 1.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	0.73 (± 3.38)	0.22 (± 7.38)		

Statistical analyses

Statistical analysis title	TFR Day 1 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	paired t-test 2 sided

Secondary: Tissue Flow Resistance on Day 0 of Infusion Site Use

End point title	Tissue Flow Resistance on Day 0 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Tissue flow resistance (TFR) observed at the infusion sites on Day 0. TFR was computed from the infusion pressure time courses measured on Day 0

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa*s/µL				
geometric mean (standard deviation)	0.42 (± 4.46)	0.49 (± 4.52)		

Statistical analyses

Statistical analysis title	TFR Day 0 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.68
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 7 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 7 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Maximum Infusion Pressure (Pmax) observed at the infusion sites on the last day of infusion site use (Day 7).

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	25.8 (± 2.11)	8.4 (± 1.42)		

Statistical analyses

Statistical analysis title	Pmax Day 7 - insulin versus placebo infusion sites
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 6 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 6 of Infusion Site Use
End point description:	
End point type	Secondary
End point timeframe: Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 6 of infusion site use.	

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	23.0 (± 1.84)	8.5 (± 1.63)		

Statistical analyses

Statistical analysis title	Pmax Day 6 - insulin versus placebo infusion sites

Statistical analysis description: Analysis was performed using paired t-test on log-transformed data	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 5 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 5 of Infusion Site Use
End point description:	
End point type	Secondary
End point timeframe: Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 5 of infusion site use.	

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	19.7 (± 1.94)	8.8 (± 1.59)		

Statistical analyses

Statistical analysis title	Pmax Day 5 - insulin versus placebo infusion sites
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 4 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 4 of Infusion Site Use
End point description:	
End point type	Secondary

End point timeframe:
Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 4 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	17.5 (± 1.84)	8.0 (± 1.60)		

Statistical analyses

Statistical analysis title	Pmax Day 4 - insulin versus placebo infusion sites

Statistical analysis description:
Analysis was performed using paired t-test on log-transformed data

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 3 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 3 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:
Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 3 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	14.1 (± 1.90)	7.9 (± 1.55)		

Statistical analyses

Statistical analysis title	Pmax Day 3 - insulin versus placebo infusion sites
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 2 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 2 of Infusion Site Use
End point description:	
End point type	Secondary
End point timeframe: Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 2 of infusion site use.	

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	11.5 (± 1.58)	8.5 (± 1.65)		

Statistical analyses

Statistical analysis title	Pmax Day 2 - insulin versus placebo infusion sites
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data.	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.006
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 1 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 1 of Infusion Site Use
End point description:	

End point type	Secondary

End point timeframe:

Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 1 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	8.7 (± 1.56)	7.5 (± 1.53)		

Statistical analyses

Statistical analysis title	Pmax Day 1 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data.

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.061
Method	paired t-test 2 sided

Secondary: Maximum Infusion Pressure on Day 0 of Infusion Site Use

End point title	Maximum Infusion Pressure on Day 0 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Maximum Infusion Pressure (Pmax) observed at the infusion sites on Day 0 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	7.4 (± 1.56)	7.2 (± 1.61)		

Statistical analyses

Statistical analysis title	Pmax Day 0 - insulin versus placebo infusion sites

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data.

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.696
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 7 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 7 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Average Infusion Pressure (Pmean) observed at the infusion sites on the last day of infusion site use (Day 7).

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	15.5 (± 2.35)	3.7 (± 1.69)		

Statistical analyses

Statistical analysis title	Pmean Day 7 - insulin versus placebo infusion site

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data.

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 6 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 6 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Average Infusion Pressure (Pmean) observed at the infusion sites on Day 6 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	13.5 (± 2.10)	3.7 (± 1.80)		

Statistical analyses

Statistical analysis title	Pmean Day 6 - insulin versus placebo infusion site

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data.

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 5 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 5 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Average Infusion Pressure (Pmean) observed at the infusion sites on Day 5 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	11.7 (± 2.31)	4.0 (± 1.78)		

Statistical analyses

Statistical analysis title	Pmean Day 5 - insulin versus placebo infusion site
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data.	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 4 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 4 of Infusion Site Use
End point description:	
End point type	Secondary
End point timeframe: Average Infusion Pressure (Pmean) observed at the infusion sites on Day 4 of infusion site use.	

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	10.7 (± 2.20)	3.7 (± 1.77)		

Statistical analyses

Statistical analysis title	Pmean Day 4 - insulin versus placebo infusion site
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data.	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 3 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 3 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Average Infusion Pressure (Pmean) observed at the infusion sites on Day 3 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	8.5 (± 2.28)	3.6 (± 1.67)		

Statistical analyses

Statistical analysis title	Pmean Day 3 - insulin versus placebo infusion site

Statistical analysis description:

Analysis was performed using paired t-test on log-transformed data.

Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 2 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 2 of Infusion Site Use

End point description:

End point type	Secondary

End point timeframe:

Average Infusion Pressure (Pmean) observed at the infusion sites on Day 2 of infusion site use.

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	5.9 (± 1.98)	3.8 (± 1.75)		

Statistical analyses

Statistical analysis title	Pmean Day 2 - insulin versus placebo infusion site
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data.	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 1 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 1 of Infusion Site Use
End point description:	
End point type	Secondary
End point timeframe: Average Infusion Pressure (Pmean) observed at the infusion sites on Day 1 of infusion site use.	

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	4.1 (± 1.54)	3.2 (± 1.59)		

Statistical analyses

Statistical analysis title	Pmean Day 1 - insulin versus placebo infusion site

Statistical analysis description: Analysis was performed using paired t-test on log-transformed data.	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.041
Method	paired t-test 2 sided

Secondary: Mean Infusion Pressure on Day 0 of Infusion Site Use

End point title	Mean Infusion Pressure on Day 0 of Infusion Site Use
End point description:	
End point type	Secondary
End point timeframe: Average Infusion Pressure (Pmean) observed at the infusion sites on Day 0 of infusion site use.	

End point values	Insulin Infusion Sites	Placebo Infusion Sites		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: kPa				
geometric mean (standard deviation)	3.4 (± 1.58)	3.7 (± 1.69)		

Statistical analyses

Statistical analysis title	Pmean Day 0 - insulin versus placebo infusion site
Statistical analysis description: Analysis was performed using paired t-test on log-transformed data.	
Comparison groups	Insulin Infusion Sites v Placebo Infusion Sites
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.62
Method	paired t-test 2 sided

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 / 30 (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	11 / 30 (36.67%)		
General disorders and administration site conditions			
insulin leakage from infusion site			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
catheter malpositioning			
subjects affected / exposed	4 / 30 (13.33%)		
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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34739179