

**Clinical trial results:****Prevention of Recurrent Severe Hypoglycaemia: a Definitive RCT Comparing Optimised MDI and CSII with or without Adjunctive Real-time Continuous Glucose Monitoring.****Summary**

EudraCT number	2009-015396-27
Trial protocol	GB
Global end of trial date	03 October 2013

Results information

Result version number	v1 (current)
This version publication date	04 August 2016
First version publication date	04 August 2016
Summary attachment (see zip file)	Hypocompass primary paper in Diabetes Care 2014 (Primary paper - Diabetes Care 2114.full text.pdf)

Trial information**Trial identification**

Sponsor protocol code	NCTU:ISRCTN52164803
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Additional study identifiers

ISRCTN number	ISRCTN52164803
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Sponsor organisation address	Freeman Hospital, Freeman Road, Newcastle upon Tyne, United Kingdom, NE7 7ND
Public contact	Professor James Shaw, Newcastle University, jim.shaw@ncl.ac.uk
Scientific contact	Professor James Shaw, Newcastle University, jim.shaw@ncl.ac.uk

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	03 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 October 2013
Global end of trial reached?	Yes
Global end of trial date	03 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate that by optimising conventional management in people with type 1 diabetes mellitus complicated by severe hypoglycaemia, rigorous prevention of biochemical hypoglycaemia will restore hypoglycaemia awareness. This was an interventional multicentre prospective randomised controlled trial comparing hypoglycaemia avoidance with optimised subcutaneous insulin analogue regimen (MDI) and insulin pump therapy (CSII) with or without adjunctive real-time continuous subcutaneous glucose monitoring (RT) in a 2x2 factorial design. This randomised controlled trial was conducted in adults with type 1 diabetes and impaired awareness of hypoglycaemia (Gold Score ≥ 4). Primary outcome was difference in 24-week Gold score.

Protection of trial subjects:

Expected serious adverse events for this study are diabetic ketoacidosis requiring inpatient hospitalisation and hypoglycaemia requiring inpatient hospitalisation. Detailed review of all six episodes of DKA reported during the study provided supporting evidence that these were at least contributed to by inter current illness. Rates of Diabetic Ketoacidosis in all interventional arms were closely monitored by the DMC (given the potential for increased risk with the study insulin replacement regimens towards hypoglycaemia reduction). However, study data showed no increased risk.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 96
Worldwide total number of subjects	96
EEA total number of subjects	96

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	88
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was a 24-week, multicentre, randomised, 2 x 2 factorial study at five UK tertiary-referral diabetes centres (Newcastle, Cambridge, Sheffield, Bournemouth and Plymouth). The recruitment period began on 1 March 2010 and was completed on 30 June 2011.

Pre-assignment

Screening details:

Patients were identified from clinics and research databases at each centre. Potential participants identified using the brief Hypoglycaemia Screening Questionnaire (hypoglycaemia history and Clarke/Edinburgh validated IAH questionnaires) to ascertain if they fulfilled severe hypoglycaemia/impaired awareness of hypoglycaemia inclusion criteria.

Pre-assignment period milestones

Number of subjects started	110 ^[1]
Intermediate milestone: Number of subjects	Consent: 110
Number of subjects completed	96 ^[2]

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Withdrew pre-randomisation: 8
Reason: Number of subjects	C-peptide positive did not meet inclusion criteria: 6

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The pre-assignment period was a wash-in period, not all subjects completed the wash-in period and were randomised hence the difference in numbers.

[2] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.

Justification: The pre-assignment period was a wash-in period, not all subjects completed the wash-in period and were randomised hence the difference in numbers.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Multiple daily injections

Arm description:

Multiple daily injections (Insulin group)

Arm type	Active comparator
Investigational medicinal product name	Insulin Aspart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

For the participants randomised to MDI (Multiple Daily Injections) Insulin Aspart will be given as follows: Formulation: 3 ml cartridge 100 Units/mL in a pre-filled pen (Flexpen).

Dosing is individual and determined in accordance with the needs of the patient. It should normally be used in combination with intermediate-acting or long-acting insulin given at least once a day. Blood

glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.

Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

For the participants randomised to MDI the glargine will be given as follows: Formulation: 3 ml cartridge 100 Units/mL in a pre-filled pen (SoloStar).

Lantus SoloStar is a pre-filled delivery device containing 3 mL insulin glargine. This device allows dose dialling in one-unit step increments between one unit and a maximum of 80 units. Lantus contains insulin glargine an insulin analogue with a prolonged duration of action. It should be administered once daily at any time but at the same time each day.

The dosage and timing of dose of Lantus should be individually adjusted.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

For the participants randomised to MDI (Multiple Daily injections) Insulin Aspart will be the rapid acting insulin analogue of choice. However for those patients who have had a previous negative experience or adverse effect with Insulin Aspart the alternative of insulin Lispro will be offered. Formulation: 3 ml cartridge 100 Units/mL in a pre-filled pen (Kwikpen).

The dosage will be determined by the physician, according to the requirement of the patient.

Arm title	CSII
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Arm description:

Continuous subcutaneous insulin infusion (Insulin regimen)

Arm type	Experimental
Investigational medicinal product name	Insulin Aspart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

For participants randomised to CSII, insulin aspart will be the insulin used. Formulation: 10 ml vial 100 Units/mL.

Dosing is individual and determined in accordance with the needs of the patient. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

For patients who have had a previous negative experience or adverse effect with Insulin Aspart the alternative of Insulin Lispro will be offered. Insulin lispro for use in the CSII group will be provided in 10ml vials 100 Units/mL.

Arm title	SMBG
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Arm description:

Self-monitoring of blood glucose

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Arm title	Real Time
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Arm description:	
Real Time Monitoring	
Arm type	Real Time Glucose Monitor
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Multiple daily injections	CSII	SMBG
Started	50	46	48
Completed	50	46	48

Number of subjects in period 1	Real Time
Started	48
Completed	48

Period 2

Period 2 title	24 weeks
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Multiple daily injections

Arm description:

Multiple daily injections (Insulin group)

Arm type	Active comparator
Investigational medicinal product name	Insulin Aspart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

For the participants randomised to MDI (Multiple Daily Injections) Insulin Aspart will be given as follows:
Formulation: 3 ml cartridge 100 Units/mL in a pre-filled pen (Flexpen).

Dosing is individual and determined in accordance with the needs of the patient. It should normally be used in combination with intermediate-acting or long-acting insulin given at least once a day. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.

Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

For the participants randomised to MDI the glargine will be given as follows: Formulation: 3 ml cartridge 100 Units/mL in a pre-filled pen (SoloStar).

Lantus SoloStar is a pre-filled delivery device containing 3 mL insulin glargine. This device allows dose dialling in one-unit step increments between one unit and a maximum of 80 units. Lantus contains insulin glargine an insulin analogue with a prolonged duration of action. It should be administered once daily at any time but at the same time each day.

The dosage and timing of dose of Lantus should be individually adjusted.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

For the participants randomised to MDI (Multiple Daily injections) Insulin Aspart will be the rapid acting insulin analogue of choice. However for those patients who have had a previous negative experience or adverse effect with Insulin Aspart the alternative of insulin Lispro will be offered. Formulation: 3 ml cartridge 100 Units/mL in a pre-filled pen (Kwikpen).

The dosage will be determined by the physician, according to the requirement of the patient.

Arm title	CSII
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Arm description:

Continuous subcutaneous insulin infusion (Insulin regimen)

Arm type	Experimental
Investigational medicinal product name	Insulin Aspart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

For participants randomised to CSII, insulin aspart will be the insulin used. Formulation: 10 ml vial 100 Units/mL.

Dosing is individual and determined in accordance with the needs of the patient. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

For patients who have had a previous negative experience or adverse effect with Insulin Aspart the alternative of Insulin Lispro will be offered. Insulin lispro for use in the CSII group will be provided in 10ml vials 100 Units/mL.

Arm title	SMBG
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Arm description:

Self-monitoring of blood glucose

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Arm title	Real Time
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Arm description:

Real Time Monitoring

Arm type	Real Time Monitoring
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Multiple daily injections	CSII	SMBG
Started	50	46	48
Completed	44	41	40
Not completed	6	5	8
Discontinued intervention - glargine intolerance	1	-	-
Did not receive intervention - too busy	-	2	-
Lost to follow-up	3	2	4
disappointed with randomisation/too busy	2	-	3
Discontinued - anxiety related to intervention	-	1	1

Number of subjects in period 2	Real Time
Started	48
Completed	45
Not completed	3
Discontinued intervention - glargine intolerance	1
Did not receive intervention - too busy	1
Lost to follow-up	1
disappointed with randomisation/too busy	-
Discontinued - anxiety related to intervention	-

Baseline characteristics

Reporting groups

Reporting group title	Multiple daily injections
Reporting group description: Multiple daily injections (Insulin group)	
Reporting group title	CSII
Reporting group description: Continuous subcutaneous insulin infusion (Insulin regimen)	
Reporting group title	SMBG
Reporting group description: Self-monitoring of blood glucose	
Reporting group title	Real Time
Reporting group description: Real Time Monitoring	

Reporting group values	Multiple daily injections	CSII	SMBG
Number of subjects	50	46	48
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)	47	41	45
From 65-84 years	3	5	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	47	50.3	47.1
standard deviation	± 12.3	± 12	± 11.8
Gender categorical Units: Subjects			
Female	34	27	28
Male	16	19	20
HbA1c Units: Subjects			
<8%	22	19	21
≥8%	28	27	27

Reporting group values	Real Time	Total	
Number of subjects	48	96	
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)	43	88	
From 65-84 years	5	8	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	50.1		
standard deviation	± 12.6	-	
Gender categorical			
Units: Subjects			
Female	33	61	
Male	15	35	
HbA1c			
Units: Subjects			
<8%	20	41	
≥8%	28	55	

End points

End points reporting groups

Reporting group title	Multiple daily injections
Reporting group description: Multiple daily injections (Insulin group)	
Reporting group title	CSII
Reporting group description: Continuous subcutaneous insulin infusion (Insulin regimen)	
Reporting group title	SMBG
Reporting group description: Self-monitoring of blood glucose	
Reporting group title	Real Time
Reporting group description: Real Time Monitoring	
Reporting group title	Multiple daily injections
Reporting group description: Multiple daily injections (Insulin group)	
Reporting group title	CSII
Reporting group description: Continuous subcutaneous insulin infusion (Insulin regimen)	
Reporting group title	SMBG
Reporting group description: Self-monitoring of blood glucose	
Reporting group title	Real Time
Reporting group description: Real Time Monitoring	

Primary: Gold Score

End point title	Gold Score
End point description:	
End point type	Primary
End point timeframe: 24 weeks	

End point values	Multiple daily injections	CSII	SMBG	Real Time
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	40	42	43
Units: Scale score				
arithmetic mean (standard deviation)	4.1 (± 1.6)	4.2 (± 1.7)	4.3 (± 1.6)	4 (± 1.7)

Statistical analyses

Statistical analysis title	Gold Score
Comparison groups	Multiple daily injections v CSII
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.76
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Statistical analysis title	Gold Score
Comparison groups	SMBG v Real Time
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard error of the mean

Secondary: Clarke Score

End point title	Clarke Score
End point description:	
End point type	Secondary
End point timeframe: 24 weeks	

End point values	Multiple daily injections	CSII	SMBG	Real Time
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	39	39	41
Units: Scale Score				
arithmetic mean (standard deviation)	3.3 (\pm 1.8)	3 (\pm 1.6)	3.3 (\pm 1.6)	3.1 (\pm 1.8)

Statistical analyses

Statistical analysis title	Clarke Score
Statistical analysis description: Insulin comparison at 24-week end point	

Comparison groups	Multiple daily injections v CSII
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31 [1]
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Notes:

[1] - a priori threshold 0.05

Statistical analysis title	Clarke Score
Comparison groups	SMBG v Real Time
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.83 [2]
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Notes:

[2] - a priori threshold 0.05

Secondary: HypoAQ

End point title	HypoAQ
End point description:	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Multiple daily injections	CSII	SMBG	Real Time
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	40	40	44
Units: Scale score				
arithmetic mean (standard deviation)	8.9 (± 4.3)	9.4 (± 4.2)	9.2 (± 4.1)	9 (± 4.4)

Statistical analyses

Statistical analysis title	HypoA-Q
Statistical analysis description:	
Hypoglycaemia awareness at 24 weeks	
Comparison groups	Multiple daily injections v CSII

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6 [3]
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Notes:

[3] - a priori threshold 0.05

Statistical analysis title	HypoA-Q
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Statistical analysis description:

Hypoglycaemia awareness at 24 weeks

Comparison groups	SMBG v Real Time
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.83 [4]
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Notes:

[4] - a priori threshold 0.05

Secondary: SH - annualised rate

End point title	SH - annualised rate
End point description:	
No. of severe hypos per patient year	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Multiple daily injections	CSII	SMBG	Real Time
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	43	44	46
Units: Patient year				
arithmetic mean (standard deviation)	1 (\pm 2.1)	0.6 (\pm 1.7)	0.9 (\pm 2.1)	0.8 (\pm 1.8)

Statistical analyses

Statistical analysis title	Severe Hypos
Statistical analysis description:	
Annualised rate	
Comparison groups	Multiple daily injections v CSII

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34 ^[5]
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Notes:

[5] - a priori threshold 0.05

Statistical analysis title	Severe Hypos
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Statistical analysis description:

Annualised rate

Comparison groups	SMBG v Real Time
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.95 ^[6]
Method	t-test, 2-sided
Parameter estimate	Group means reported elsewhere
Variability estimate	Standard deviation

Notes:

[6] - a priori threshold 0.05

Secondary: SH - number affected

End point title	SH - number affected
End point description: Severe hypos number affected	
End point type	Secondary
End point timeframe: 24 weeks	

End point values	Multiple daily injections	CSII	SMBG	Real Time
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	43	44	46
Units: Number of individuals affected by SH	11	7	9	9

Statistical analyses

Statistical analysis title	SH number affected
Comparison groups	Multiple daily injections v CSII

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.399
Method	Chi-squared

Statistical analysis title	SH number affected
Comparison groups	SMBG v Real Time
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.92
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period during which adverse events were reported from the beginning of the RCT to the end of the randomised control trial period at 24 weeks.

Assessment type	Systematic
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Dictionary used

Dictionary name	As reported verbatim
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Dictionary version	1.0
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Reporting groups

Reporting group title	Multiple daily injections (MDI)
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Reporting group description:

Multiple daily injections

Reporting group title	CSII
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Reporting group description:

Continuous subcutaneous insulin infusion

Serious adverse events	Multiple daily injections (MDI)	CSII	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 50 (12.00%)	11 / 46 (23.91%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Raised eye pressure			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Gastroenteritis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot ulceration			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetic ketoacidosis			
subjects affected / exposed	2 / 50 (4.00%)	4 / 46 (8.70%)	
occurrences causally related to treatment / all	2 / 2	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fracture of tibia and fibula			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture of radius			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic arthritis in shoulder joint			

subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Multiple daily injections (MDI)	CSII	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 50 (28.00%)	11 / 46 (23.91%)	
Injury, poisoning and procedural complications			
Fall	Additional description: Slipped in garden and fell, swollen left ankle, bruising to right arm and painful ribs on right side.		
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Low blood pressure			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences (all)	1	0	
Mini stroke			
subjects affected / exposed	1 / 50 (2.00%)	0 / 46 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Meralgia paraesthetica			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences (all)	0	1	
Carpal tunnel decompression	Additional description: left side		
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences (all)	0	1	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Inflammation at injection site			
subjects affected / exposed	0 / 50 (0.00%)	1 / 46 (2.17%)	
occurrences (all)	0	1	
Bleeding at injection site			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Bruising at IPRO/sensor site subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	1 / 46 (2.17%) 1	
Finger cellulitis subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 46 (0.00%) 0	
Small raised red area after sensor is removed subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 46 (0.00%) 0	
Blister and ulceration of right toe subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 46 (0.00%) 0	
Gastrointestinal disorders			
Viral gastrointestinal infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Mouth ulcer subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 46 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 46 (0.00%) 0	
Ulceration subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Renal and urinary disorders			
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Endocrine disorders			
Hypoglycaemia resulting in fall subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 46 (0.00%) 0	

Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Infections and infestations			
Viral infection subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	1 / 46 (2.17%) 1	
Infected toe subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Chest infection subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	2 / 46 (4.35%) 2	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Shingles subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	
Product issues			
Veo pump screen froze	Additional description: New pump required		
subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	1 / 46 (2.17%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 April 2010	Change of Principal Investigator at the Bournemouth site from Dr David Kerr to Dr Joseph Begley
08 July 2010	Clarification of details for reporting of adverse events and minor changes to the statistical analysis plan in the protocol.
21 December 2011	Addition of qualitative interview sub study for some hypoCompass study participants at the end of the RCT period.
30 July 2013	Change of Principal Investigator at the Bournemouth site from Dr Joseph Begley (now retired) to Professor David Kerr.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported