Clinical trial results:
A Phase 3, Randomized, Active Comparator, Double-Blind, Multi-Center Study to Compare the Efficacy, Safety and Tolerability of ITCA 650 to Sitagliptin as Add-on Therapy to Metformin in Patients with Type 2 Diabetes

Summary

EudraCT number	2012-002117-19
Trial protocol	LV DK DE
Global end of trial date	07 July 2015

Results information

Result version number	v1 (current)
This version publication date	14 August 2016
First version publication date	14 August 2016

Trial information

Trial identification

Sponsor protocol code	ITCA 650-CLP-105

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01455870
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intarcia Therapeutics, Inc
Sponsor organisation address	24650 Industrial Blvd, Hayward, CA, United States, 94545
Public contact	Chief Medical Officer, Intarcia Therapeutics, Inc, +1 617.936.2500, medinfo@intarcia.com
Scientific contact	Chief Medical Officer, Intarcia Therapeutics, Inc, +1 617.936.2500, medinfo@intarcia.com

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	07 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2015
Global end of trial reached?	Yes
Global end of trial date	07 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate that ITCA 650 is non-inferior to sitagliptin in reducing HbA1c in patients with type 2 diabetes following 52 weeks of treatment. The noninferiority margin was 0.3%. If non-inferiority is demonstrated, then ITCA 650 will be tested for superiority in reducing HbA1c.

Protection of trial subjects:

The study protocol, all study protocol amendments, written study patient information, informed consent form (ICF), and any other appropriate study-related information were reviewed and approved by an independent ethics committee (IEC) or institutional review board (IRB) at each study site. All subjects were free to withdraw from the clinical trial at any time for any reason given. Protocol pre-defined reasons for discontinuation were the following: (1) Patient withdraws consent or requests discontinuation from the study for any reason; (2) Sponsor discontinues the study; (3) Pregnancy; (4) Occurrence of a clinical or laboratory AE, either serious or non serious, at the discretion of the Investigator; (5) Need to initiate therapy with an excluded concomitant medication; (6) Permanent discontinuation of study medication; (7) Any medical condition or personal circumstance that, in the opinion of the Investigator, exposes the patient to risk by continuing in the study or precludes adherence to the protocol; (8) Loss of glucose control. Close medical monitoring of all subjects was adhered to throughout the trial duration. An independent safety monitor evaluated safety information on a continuous basis in a blinded fashion. Patients who experienced hyperglycemia were prescribed rescue therapy as described in the protocol.

Background therapy:

Metformin, at least ≥1500 mg/day oral.

Evidence for comparator:

The choice of a control group with an active comparator (sitagliptin) was justified because it allowed all participants to receive active treatment. Sitagliptin is an approved pharmacotherapy for the treatment of type 2 diabetes worldwide and has a well characterized safety and efficacy profile.

Actual start date of recruitment	13 May 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	Denmark: 18
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Latvia: 19
Country: Number of subjects enrolled	United States: 321
Country: Number of subjects enrolled	Israel: 9

Country: Number of subjects enrolled	South Africa: 37
Country: Number of subjects enrolled	Croatia: 18
Country: Number of subjects enrolled	Mexico: 45
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Malaysia: 15
Country: Number of subjects enrolled	Saudi Arabia: 1
Worldwide total number of subjects	535
EEA total number of subjects	73

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)	448
From 65 to 84 years	87
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One hundred and twenty four global investigational sites were involved in the recruitment and treatment of 535 and patients.

Pre-assignment

Screening details:

Eligible subjects were males and females age 18 to 80 years inclusive with a diagnosis of type 2 diabetes for ≥ 3 months. Subjects also had HbA1c ≥7.5% and ≤10.5% and a body mass index (BMI) ≥25 kg/m2 and ≤45 kg/m2.

Period 1

Period 1 title	Overall study (D0 - Week 52) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: ITCA 650

Arm description:

Group 1: ITCA 650 osmotic mini-pump placed sub-dermally. ITCA 650 was combined with an oral placebo to maintain the blind.

Arm type	Experimental
Investigational medicinal product name	ITCA 650 20 mcg/day
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Subcutaneous use

Dosage and administration details:

From randomization to Week 13, subjects receive 20 mcg/day of ITCA 650. From week 13 to week 52, subjects receive 60 mcg/day of ITCA 650. Subjects also take oral placebo for treatment period duration to maintain the blind between treatment groups.

Investigational medicinal product name	ITCA 650 60 mcg/day
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Subcutaneous use

Dosage and administration details:

From randomization to Week 13, subjects receive 20 mcg/day of ITCA 650. From week 13 to week 52, subjects receive 60 mcg/day of ITCA 650. Subjects also take oral placebo for treatment period duration to maintain the blind between treatment groups.

Arm title	Group 2: Sitagliptin

Arm description:

Sitagliptin 100 mg/day, oral administration. Group 2 subjects received an ITCA placebo device to maintain the blind.

Arm type	Active comparator

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin 100 mg/day plus ITCA placebo.

Number of subjects in period 1[1]	Group 1: ITCA 650	Group 2: Sitagliptin
Started	265	265
Completed	204	217
Not completed	61	48
Patients who did not complete treatment	61	48

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Five of the enrolled subjects (all enrolled in the UNITED STATES) were never treated so although 535 subjects were randomized, only 530 actually received treatment and entered the treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: ITCA 650
Reporting group description:	
Group 1: ITCA 650 osmotic mini-pump placed sub-dermally. ITCA 650 was combined with an oral placebo to maintain the blind.	
Reporting group title	Group 2: Sitagliptin
Reporting group description:	
Sitagliptin 100 mg/day, oral administration. Group 2 subjects received an ITCA placebo device to maintain the blind.	

Reporting group values	Group 1: ITCA 650	Group 2: Sitagliptin	Total
Number of subjects	265	265	530
Age categorical			
Units: Subjects			
Adults (18-64 years)	220	223	443
From 65-84 years	45	42	87
Age continuous			
Units: years			
arithmetic mean	55.4	54.6	
standard deviation	± 9.84	± 10.32	-
Gender categorical			
Units: Subjects			
Female	120	107	227
Male	145	158	303

End points

End points reporting groups

Reporting group title	Group 1: ITCA 650
Reporting group description:	
Group 1: ITCA 650 osmotic mini-pump placed sub-dermally. ITCA 650 was combined with an oral placebo to maintain the blind.	
Reporting group title	Group 2: Sitagliptin
Reporting group description:	
Sitagliptin 100 mg/day, oral administration. Group 2 subjects received an ITCA placebo device to maintain the blind.	

Primary: Change in HbA1c (%) between Week 52 and Day 0

End point title	Change in HbA1c (%) between Week 52 and Day 0
End point description:	
Calculated as: Value of HbA1c (%) at Week 52 - Hba1c at baseline (%) (mITT population).	
End point type	Primary
End point timeframe:	
The primary efficacy variable is the change in HbA1c (%) between baseline and Week 52 from the mITT population.	

End point values	Group 1: ITCA 650	Group 2: Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263	257		
Units: Change from Baseline HbA1c (%)				
least squares mean (standard error)	-1.47 (± 0.08)	-0.76 (± 0.08)		

Statistical analyses

Statistical analysis title	Change in HbA1c (%) between Week 52 and Day 0
Statistical analysis description:	
Mixed Model Repeated Measures (MMRM) was used to compare the ITCA 650 treatment group to the sitagliptin treatment group. In the model, change from baseline HbA1c through Week 52 was the outcome variable. Treatment group, visit, and the interaction between treatment and visit were fixed effects. Baseline HbA1c was the covariate.	
Comparison groups	Group 1: ITCA 650 v Group 2: Sitagliptin
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (final values)
Point estimate	-0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	-0.49

Notes:

[1] - 0.3 % inferiority margin.

Secondary: Composite HbA1c/Weight Reduction

End point title	Composite HbA1c/Weight Reduction

End point description:

Proportion of patients with decrease in HbA1c >0.5% and weight loss ≥2 kg between Week 52 and Day 0.

End point type	Secondary

End point timeframe:

Proportion of patients who achieved Composite HbA1c/Weight Reduction at Week 52.

End point values	Group 1: ITCA 650	Group 2: Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171[2]	126[3]		
Units: Not Applicable				
Achieved	104	35		
Not Achieved	67	91		

Notes:

[2] - 171 evaluable subjects from ITCA 650 group, mITT population

[3] - 126 evaluable subjects from sitagliptin group, mITT population

Statistical analyses

Statistical analysis title	Composite HbA1c/Weight Reduction

Statistical analysis description:

The ITCA 650 treatment group was compared to the sitagliptin treatment group using a logistic regression model with proportion of patients with HbA1c reduction > 0.5% and weight loss >= 2kg from baseline at Week 52 as the outcome variable, and treatment as a factor and baseline HbA1c (%) and baseline body weight as covariates.

Comparison groups	Group 1: ITCA 650 v Group 2: Sitagliptin
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	5.6

Secondary: Change in body weight between Week 52 and Day 0	
End point title	Change in body weight between Week 52 and Day 0
End point description: Change in weight (kg) from baseline - 52 week time point.	
End point type	Secondary
End point timeframe: Change in weight (kg) from baseline - 52 week time point.	

End point values	Group 1: ITCA 650	Group 2: Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263	257		
Units: kilogram(s)				
least squares mean (standard error)	-3.97 (± 0.33)	-1.25 (± 0.35)		

Statistical analyses

Statistical analysis title	Change in body weight between Week 52 and Day 0
Comparison groups	Group 2: Sitagliptin v Group 1: ITCA 650
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (final values)
Point estimate	-2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.66
upper limit	-1.77

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment emergent adverse events (Day 0 - End of study).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	Group 1: ITCA 650
Reporting group description:	
Group 1: ITCA 650 osmotic mini-pump placed sub-dermally. ITCA 650 plus oral placebo (to maintain blind between treatment groups).	
Reporting group title	Group 2: Sitagliptin
Reporting group description:	
Group 2: Sitagliptin 100 mg/day plus ITCA placebo.	

Serious adverse events	Group 1: ITCA 650	Group 2: Sitagliptin	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 265 (5.66%)	20 / 265 (7.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm of unknown primary site			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucinous cystadenocarcinoma ovary			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Deep Vein Thrombosis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depession			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			

subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Congestive Heart Failure			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 265 (0.75%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 265 (0.38%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	0 / 265 (0.00%)	2 / 265 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina unstable			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
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			
Skin ulcer			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			

subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 265 (0.38%)	0 / 265 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 265 (0.75%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 265 (0.00%)	1 / 265 (0.38%)	
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: 5 %

Non-serious adverse events	Group 1: ITCA 650	Group 2: Sitagliptin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	146 / 265 (55.09%)	112 / 265 (42.26%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	14 / 265 (5.28%)	7 / 265 (2.64%)	
occurrences (all)	14	7	
Headache			
subjects affected / exposed	21 / 265 (7.92%)	21 / 265 (7.92%)	
occurrences (all)	24	26	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	30 / 265 (11.32%)	19 / 265 (7.17%)	
occurrences (all)	36	23	
Gastrooesophageal reflux disease			
subjects affected / exposed	15 / 265 (5.66%)	5 / 265 (1.89%)	
occurrences (all)	16	6	
Nausea			
subjects affected / exposed	83 / 265 (31.32%)	36 / 265 (13.58%)	
occurrences (all)	119	40	
Vomiting			
subjects affected / exposed	51 / 265 (19.25%)	14 / 265 (5.28%)	
occurrences (all)	76	15	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 265 (2.64%)	16 / 265 (6.04%)	
occurrences (all)	9	20	
Upper respiratory tract infection			
subjects affected / exposed	18 / 265 (6.79%)	24 / 265 (9.06%)	
occurrences (all)	21	30	
Urinary tract infection			
subjects affected / exposed	25 / 265 (9.43%)	17 / 265 (6.42%)	
occurrences (all)	32	24	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	5 / 265 (1.89%)	14 / 265 (5.28%)	
occurrences (all)	6	15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2012	Changes to study design, additional clarification to some study procedures.
10 September 2013	Updates to the I/E criteria and safety procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported