# Clinical trial results:
# A double blind placebo controlled study to evaluate the effect of bexagliflozin tablets on hemoglobin A1c in patients with type 2 diabetes mellitus and moderate renal impairment

## Summary

| | |
|---|---|
| EudraCT number | 2016-002580-34 |
| Trial protocol | ES |
| Global end of trial date | 11 January 2018 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 23 August 2019 |
| First version publication date | 23 August 2019 |
| Summary attachment (see zip file) | THR-1442-C-448 Synopsis (thr-1442-c-448-synopsis.pdf) |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | THR-1442-C-448 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02836873 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | EMA: UPI number 498543 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Theracos Sub, LLC |
| Sponsor organisation address | 225 Cedar Hill St, Marlborough, MA, United States, 01752 |
| Public contact | Clinical Trial Project Management, Translational Medicine Group, 001 5086884221, info@theracos.com |
| Scientific contact | Clinical Trial Project Management, Translational Medicine Group, 001 6176430699, info@theracos.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 | 20 August 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 11 January 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 January 2018 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the efficacy of bexagliflozin on lowering HbA1c in patients with type 2 diabetes mellitus and moderate renal impairment.

Protection of trial subjects:

During the run-in period, subjects received diet and exercise counseling and instructions on contacting the clinic in the event of hypoglycemia, hyperglycemia, or symptoms that may suggest ketoacidosis. Subjects were trained to use the glucometer and record any events in the glycemic control diary. Health status of subjects were reviewed regularly by review of adverse events (AEs), concomitant medications use, vital signs, electrocardiograms (ECGs), and results from physical examinations and blood and urine specimen collections. At every visit, including the phone interviews, participants were queried regarding AEs and information on all events that potentially represent diabetic ketoacidosis (DKA) or major adverse cardiovascular events. Following the exit visit, subjects were advised to see their primary physician to
undergo treatment to control their diabetes and cardiovascular conditions.
Subjects with hyperglycemia based on blood glucose levels during the treatment period received, at the Investigator's discretion, approved anti-diabetic medication. In addition, adjustment by the investigator to the pre-screening anti-diabetic therapies were recommended if hypoglycemia occurred.
Evaluation and management of subjects with and at risk for acute kidney injury (AKI) were performed during the study period based on the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline in 2012.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 September 2016 |
| 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 | Japan: 116 |
| Country: Number of subjects enrolled | United States: 103 |
| Country: Number of subjects enrolled | Spain: 65 |
| Country: Number of subjects enrolled | France: 28 |
| Worldwide total number of subjects | 312 |
| EEA total number of subjects | 93 |

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) | 77 |
| From 65 to 84 years | 232 |
| 85 years and over | 3 |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment occurred between 23 Sep 2016 and 14 Jun 2017. Subjects were recruited from France, Spain, Japan and the United States.

### Pre-assignment

Screening details:

Screening criteria include male or non-pregnant female ≥ 20 years of age with diagnosis of T2DM with HbA1c between 7.0% and 10.5% and stage 3 CKD (eGFR ≥ 30 and< 60 mL min^-1 per 1.73 m^2. All eligible subjects entered a one week run-in period. Subjects compliant in taking run-in medication and had stable eGFR were eligible for randomization.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Blinding implementation details:

Placebo tablets were produced to match bexagliflozin tablets, 20 mg. Laboratory test urine glucose values were blinded to study team.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Bexagliflozin |

Arm description:

Each subject will receive a bexagliflozin tablet, 20 mg, once daily for the duration of the study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bexagliflozin tablets, 20 mg |
| Investigational medicinal product code | |
| Other name | EGT0001442, EGT0001474 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablet for once daily oral administration

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Each subject will receive a placebo (inactive) tablet once daily for the duration of the study.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Inactive tablet to match the active bexagliflozin tablet, 20 mg, for once daily oral administration

| **Number of subjects in period 1** | Bexagliflozin | Placebo |
|---|---|---|
| Started | 157 | 155 |
| Completed | 152 | 144 |
| Not completed | 5 | 11 |
| Consent withdrawn by subject | 2 | 2 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 1 | 4 |
| Subject moved | 1 | - |
| Lost to follow-up | 1 | 3 |
| Protocol deviation | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Bexagliflozin |
| Reporting group description: | |
| Each subject will receive a bexagliflozin tablet, 20 mg, once daily for the duration of the study. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Each subject will receive a placebo (inactive) tablet once daily for the duration of the study. | |

| Reporting group values | Bexagliflozin | Placebo | Total |
|---|---|---|---|
| Number of subjects | 157 | 155 | 312 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | | | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 69.3 | 69.9 | |
| standard deviation | ± 8.36 | ± 8.29 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 65 | 51 | 116 |
| Male | 92 | 104 | 196 |
| Race<br>Units: Subjects | | | |
| White | 83 | 88 | 171 |
| Black or African-American | 9 | 6 | 15 |
| Asian | 61 | 59 | 120 |
| American Indian/Alaskan Native | 0 | 0 | 0 |
| Native Hawaiian/Other Pacific Islander | 2 | 0 | 2 |
| Other | 2 | 2 | 4 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 7 | 17 | 24 |
| Not Hispanic or Latino | 149 | 138 | 287 |
| Not Reported | 1 | 0 | 1 |
| Country of Investigational Site<br>Units: Subjects | | | |
| France | 12 | 16 | 28 |
| Spain | 34 | 31 | 65 |
| Japan | 58 | 58 | 116 |
| USA | 53 | 50 | 103 |
| SBP<br>Units: mm Hg | | | |
| arithmetic mean | 135.9 | 137.6 | |
| standard deviation | ± 14.25 | ± 14.75 | - |
| HbA1c<br>Units: Percent | | | |

| | | | |
|---|---|---|---|
| arithmetic mean | 8.01 | 7.95 | |
| standard deviation | ± 0.786 | ± 0.812 | - |
| FPG | | | |
| Units: mmol/L | | | |
| arithmetic mean | 8.61 | 8.63 | |
| standard deviation | ± 2.525 | ± 2.246 | - |
| eGFR | | | |
| Units: mL min-1 per 1.73 m2 | | | |
| arithmetic mean | 45.44 | 44.78 | |
| standard deviation | ± 8.565 | ± 8.085 | - |
| UACR | | | |
| Units: mg/g | | | |
| arithmetic mean | 355.3 | 510.0 | |
| standard deviation | ± 776.77 | ± 1094.46 | - |
| Duration of Diabetes | | | |
| Units: Years | | | |
| arithmetic mean | 15.54 | 16.28 | |
| standard deviation | ± 9.198 | ± 8.977 | - |
| Duration of CKD | | | |
| Units: years | | | |
| arithmetic mean | 4.92 | 5.02 | |
| standard deviation | ± 3.926 | ± 4.99 | - |
| Body Weight | | | |
| Units: kg | | | |
| arithmetic mean | 82.90 | 82.59 | |
| standard deviation | ± 20.509 | ± 21.196 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Bexagliflozin |
| Reporting group description: | |
| Each subject will receive a bexagliflozin tablet, 20 mg, once daily for the duration of the study. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Each subject will receive a placebo (inactive) tablet once daily for the duration of the study. | |

### Primary: Change from Baseline in HbA1c at Week 24

| | |
|---|---|
| End point title | Change from Baseline in HbA1c at Week 24 |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| 24 weeks | |

| End point values | Bexagliflozin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 157 | 155 | | |
| Units: Percent | | | | |
| least squares mean (confidence interval 95%) | -0.59 (-0.72 to -0.46) | -0.31 (-0.44 to -0.18) | | |

### Statistical analyses

| Statistical analysis title | Difference of LS Means from Placebo |
|---|---|
| Statistical analysis description: | |
| Model-adjusted using mixed effects repeated measures analysis | |
| Comparison groups | Bexagliflozin v Placebo |
| Number of subjects included in analysis | 312 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0026 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.46 |
| upper limit | -0.1 |

## Secondary: Change in Body Weight from Baseline to Week 24 in Subjects with BMI >= 25 kg/m2

| | |
|---|---|
| End point title | Change in Body Weight from Baseline to Week 24 in Subjects with BMI >= 25 kg/m2 |

End point description:

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

24 weeks

| End point values | Bexagliflozin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 125[1] | 122[2] | | |
| Units: kg | | | | |
| least squares mean (confidence interval 95%) | -2.31 (-2.84 to -1.79) | -0.55 (-1.08 to -0.02) | | |

Notes:

[1] - Subject with BMI >= 25 kg/m2

[2] - Subject with BMI >= 25 kg/m2

### Statistical analyses

| Statistical analysis title | Difference of LS Means from Placebo |
|---|---|
| Comparison groups | Bexagliflozin v Placebo |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | -1.03 |

## Secondary: Change in SBP from Baseline to Week 24 in Subject with Baseline SBP >= 130 mm Hg

| | |
|---|---|
| End point title | Change in SBP from Baseline to Week 24 in Subject with Baseline SBP >= 130 mm Hg |

End point description:

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

24 weeks

| **End point values** | Bexagliflozin | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 107[3] | 113[4] | | |
| Units: mm Hg | | | | |
| least squares mean (confidence interval 95%) | -10.14 (-13.05 to -7.23) | -7.51 (-10.39 to -4.63) | | |

Notes:

[3] - Subject with baseline SBP >= 130 mm Hg

[4] - Subjects with baseline SBP >= 130 mm Hg

## Statistical analyses

| **Statistical analysis title** | Difference of LS Means from Placebo |
|---|---|
| Comparison groups | Bexagliflozin v Placebo |
| Number of subjects included in analysis | 220 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2035 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.7 |
| upper limit | 1.44 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: 24 weeks | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Bexagliflozin |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Serious adverse events | Bexagliflozin | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 157 (7.01%) | 9 / 155 (5.81%) | |
| 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) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric cancer | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Vascular disorders | | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Bundle branch block left | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carotid artery disease | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Deafness unilateral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| 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 | | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| 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 / 157 (0.00%) | 1 / 155 (0.65%) | |
| 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 | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathic arthropathy | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | Bexagliflozin | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 109 / 157 (69.43%) | 105 / 155 (67.74%) | |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 6 / 157 (3.82%) | 3 / 155 (1.94%) | |
| occurrences (all) | 7 | 3 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 3 / 155 (1.94%) | |
| occurrences (all) | 5 | 3 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 3 / 155 (1.94%) | |
| occurrences (all) | 5 | 3 | |
| Hypertension | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 0 / 155 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 7 / 157 (4.46%) | 11 / 155 (7.10%) | |
| occurrences (all) | 7 | 12 | |
| Constipation | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 6 / 155 (3.87%) | |
| occurrences (all) | 3 | 6 | |
| Renal and urinary disorders | | | |
| Polyuria | | | |
| subjects affected / exposed | 11 / 157 (7.01%) | 4 / 155 (2.58%) | |
| occurrences (all) | 14 | 4 | |
| Acute kidney injury | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 6 / 155 (3.87%) | |
| occurrences (all) | 9 | 6 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 5 / 155 (3.23%) | |
| occurrences (all) | 11 | 5 | |
| Back pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 157 (3.18%) | 3 / 155 (1.94%) | |
| occurrences (all) | 5 | 3 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 11 / 157 (7.01%) | 12 / 155 (7.74%) | |
| occurrences (all) | 12 | 18 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 9 / 157 (5.73%) | 5 / 155 (3.23%) | |
| occurrences (all) | 10 | 5 | |
| Bronchitis | | | |
| subjects affected / exposed | 7 / 157 (4.46%) | 2 / 155 (1.29%) | |
| occurrences (all) | 7 | 2 | |
| Sinusitis | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 0 / 155 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 39 / 157 (24.84%) | 38 / 155 (24.52%) | |
| occurrences (all) | 239 | 249 | |
| Polydipsia | | | |
| subjects affected / exposed | 7 / 157 (4.46%) | 2 / 155 (1.29%) | |
| occurrences (all) | 10 | 2 | |

## 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/31101403