Clinical trial results:
Effects of dapagliflozin treatment on urinary proteomic patterns in patients with type 2 diabetes

Summary

EudraCT number	2015-000335-32
Trial protocol	DK
Global end of trial date	29 August 2017

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	2015-01-21

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Steno Diabetes Center Copenhagen
Sponsor organisation address	Borgmester Ib Juuls vej 83, Herlev, Denmark, DK-2730
Public contact	Diabetes Complications Research, Steno Diabetes Center Copenhagen, +45 30797028, peter.rossing@regionh.dk
Scientific contact	Diabetes Complications Research, Steno Diabetes Center Copenhagen, +45 27512622, frederik.persson@regionh.dk

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	21 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 August 2017
Global end of trial reached?	Yes
Global end of trial date	29 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of dapagliflozin treatment on urinary proteomic patterns in patients with type 2 diabetes, microalbuminuria, and eGFR above 60 ml/min/1.73m2

Protection of trial subjects:

Participants could contact trial investigators directly by phone

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2015
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	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	37
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We included 77 patients out of which 37 failed screening mainly because of UACR <30 mg/g and HbA1C ≤ 58 mmol/mol. Thus, 40 patients were randomized to dapagliflozin or placebo

Pre-assignment

Screening details:

We included 77 patients out of which 37 failed screening mainly because of UACR <30 mg/g and HbA1C ≤ 58 mmol/mol. Thus, 40 patients were randomized to dapagliflozin or placebo .

Period 1

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

Blinding implementation details:

After screening, participants were randomized to dapagliflozin 10 mg once daily added to standard treatment or matching placebo in a 1:1 ratio. After 12 weeks participants continued with the opposite treatment for another 12 weeks

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

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

Dosage and administration details:

10 mg once daily

Arm title	Dapagliflozin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	dapagliflozin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg once daily

Number of subjects in period 1	Placebo	Dapagliflozin
Started	20	20
Completed	16	20
Not completed	4	0
Adverse event, non-fatal	2	-
Death	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Randomized treatment

Reporting group description: -

Reporting group values	Randomized treatment	Total	
Number of subjects	40	40	
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)	37	37	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	64		
standard deviation	± 8	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	36	36	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Dapagliflozin
Reporting group description: -	
Subject analysis set title	Dapagliflozin
Subject analysis set type	Intention-to-treat
Subject analysis set description: Active treatment group	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Placebo treatment period	

Primary: Change in CKD273 score

End point title	Change in CKD273 score
End point description: Dapagliflozin treatment significantly decreased (improved) the CKD273 score with 0.22 (95% Ci: 0.09 – 0.36, p >0.01)	
End point type	Primary
End point timeframe: During the 12 weeks treatment period	

End point values	Dapagliflozin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32[1]	32[2]		
Units: units				
number (confidence interval 95%)	0.462 (0.352 to 0.572)	0.231 (0.136 to 0.326)		

Notes:

[1] - Due to lacking urine collections

[2] - Due to lacking urine collections

Statistical analyses

Statistical analysis title	Linear mixed model
Statistical analysis description: linear mixed effect model using treatment, sequence, and period as fixed effects using random intercepts for participants	
Comparison groups	Dapagliflozin v Placebo

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the course of the study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Adverse events

Reporting group description: -

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 40 (12.50%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Atrial fibrillation			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Elevated troponins/ CABG			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Collapsed lung			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Cardiac decompensation			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Genital pain			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Renal and urinary disorders Increased diuresis subjects affected / exposed occurrences (all)	 6 / 40 (15.00%) 6		
Musculoskeletal and connective tissue disorders Collapsed hip prostethesis subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 1 / 40 (2.50%) 1 1 / 40 (2.50%) 1		
Infections and infestations Genital infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) Other infections subjects affected / exposed occurrences (all)	 9 / 40 (22.50%) 9 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2 6 / 40 (15.00%) 6		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 3 / 40 (7.50%) 3		

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