Clinical trial results:
The effects of SGLT2-inhibition in patients with type 2 diabetes and preserved kidney function on renal hemodynamics, kidney function and vasoactive hormones

Summary

EudraCT number	2019-004303-12
Trial protocol	DK
Global end of trial date	08 July 2022

Results information

Result version number	v1 (current)
This version publication date	22 February 2025
First version publication date	22 February 2025

Trial information

Trial identification

Sponsor protocol code	SFN-1-2019

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University Clinic of Nephrology and Hypertension, Regional Hospital Holstebro
Sponsor organisation address	Lægårdvej 12, Holstebro, Denmark,
Public contact	Steffen Flindt Nielsen, University Clinic of Nephrology and Hypertension, Regional Hospital Holstebro, 0045 78436588, steffen.nielsen@midt.rm.dk
Scientific contact	Steffen Flindt Nielsen, University Clinic of Nephrology and Hypertension, Regional Hospital Holstebro, 0045 78436588, steffen.nielsen@midt.rm.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	08 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2022
Global end of trial reached?	Yes
Global end of trial date	08 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To examine the effects of SGLT2-inhibition versus placebo on renal hemodynamics in patients with typ2 diabetes and preserved kidney function.
The trial was a double blind, randomized controlled cross over trial where each participant was randomized to 4 weeks of treatment with empagliflozin 10 mg per day and matching placebo in random order.

Protection of trial subjects:

All participants signed informed consent

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 May 2021
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	6
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion and exclusion criterias have been specified at the beginning of the trial. 22 patients were screened, 4 were screen failures. 2 patients did not complete the study. 16 completed

Period 1

Period 1 title	Treament period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Empagliflozin

Arm description:

Crossed over design

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

Dosage and administration details:

10 mg x day

Number of subjects in period 1	Empagliflozin
Started	18
Completed	16
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Period 2

Period 2 title	Placebo period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

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:

1 tablet each day, identical to Empagliflozin except active treatment

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: This is a crossed over trial

Number of subjects in period 2[2]	Placebo
Started	16
Completed	16

Notes:

[2] - 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: This is a crossover trial

Baseline characteristics

Reporting groups	
Reporting group title	Placebo period

Reporting group description: -

Reporting group values	Placebo period	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	68.0		
standard deviation	± 8.5	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	5	5	

End points

End points reporting groups

Reporting group title	Empagliflozin
Reporting group description: Crossed over design	
Reporting group title	Placebo
Reporting group description: -	

Primary: Renal Blood Flow

End point title	Renal Blood Flow
End point description:	
End point type	Primary
End point timeframe: meassured at the end of each treatment period	

End point values	Empagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: ml/min/ccm				
geometric mean (inter-quartile range (Q1-Q3))	1.52 (1.27 to 1.85)	1.57 (1.33 to 1.90)		

Statistical analyses

Statistical analysis title	paired t-test
Comparison groups	Placebo v Empagliflozin
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.29
Method	t-test, 2-sided

Secondary: GFR

End point title	GFR
End point description:	
End point type	Secondary

End point timeframe:
at the end of each treatment period

End point values	Empagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: ml/min/1.73m2				
geometric mean (inter-quartile range (Q1-Q3))	75.6 (66.7 to 94.3)	97.6 (78.9 to 102.7)		

Statistical analyses

Statistical analysis title	paired t-test
Comparison groups	Placebo v Empagliflozin
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided

Secondary: systolic blood pressure

End point title	systolic blood pressure

End point description:

End point type	Secondary

End point timeframe:
meassured at the end of each period

End point values	Empagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mmHg				
arithmetic mean (standard deviation)	131 (± 12)	135 (± 9)		

Statistical analyses

Statistical analysis title	paired t-test
Comparison groups	Placebo v Empagliflozin

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	t-test, 2-sided

Secondary: diastolic blood pressure

End point title	diastolic blood pressure

End point description:

End point type	Secondary

End point timeframe:
meassured at the end of each period

End point values	Empagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mmHg				
arithmetic mean (standard deviation)	77 (± 10)	79 (± 8)		

Statistical analyses

Statistical analysis title	paired t-test
Comparison groups	Placebo v Empagliflozin
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	t-test, 2-sided

Secondary: TVR

End point title	TVR

End point description:

End point type	Secondary

End point timeframe:
meassured at the end of each period

End point values	Empagliflozin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: dyn/s*m5				
arithmetic mean (standard deviation)	1781 (± 130)	1829 (± 131)		

Statistical analyses

Statistical analysis title	paired t-test
Comparison groups	Placebo v Empagliflozin
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the beginning of the trial to LPLV + 1 week	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21
Reporting groups	
Reporting group title	total trial

Reporting group description: -

Serious adverse events	total trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	total trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 18 (50.00%)		
Vascular disorders			
Aneurysm	Additional description: Abdominal aortic aneurism detected during a CT scan		
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
General disorders and administration site conditions			
Dizziness			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Headache			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Immune system disorders			
Myasthenia gravis	Additional description: Worsening of known myastenia		
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Endocrine disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Muscle discomfort			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Muscle contusion			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vaginal infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Balanitis candida			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

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/39810756