Clinical trial results:
The effect of spironolactone on renal hemodynamics in patients with essential hypertension

Summary

EudraCT number	2019-001636-60
Trial protocol	DK
Global end of trial date	09 June 2021

Results information

Result version number	v1 (current)
This version publication date	03 September 2022
First version publication date	03 September 2022

Trial information

Trial identification

Sponsor protocol code	SL-3-2019

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University Clinic in Nephrology and Hypertension
Sponsor organisation address	Hospitalsparken 15, Herning, Denmark, 7400
Public contact	Stine Sundgaard Langaa, University clinic of Nephrology and Hypertension, Gødstrup Hospital, 0045 60125230, stinlg@rm.dk
Scientific contact	Jesper Nørgaard Bech, University clinic of Nephrology and Hypertension, Gødstrup Hospital, 0045 78436587, jesper.noergaard.bech@vest.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	12 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 June 2021
Global end of trial reached?	Yes
Global end of trial date	09 June 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect af treatment with spironolactone for 4 weeks renal hemodynamics in patients with essentiel hypertension

Protection of trial subjects:

Initiation of blood pressure medication (metoprololsuccinate), if ambulatory blood pressure measured approximately 2 weeks after cessation of antihypertensiva exceeded 150/95.
Blood test approx. 2 weeks into each 4-week treatment period

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 September 2019
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	7
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited by advertisement in the local newspaper

Pre-assignment

Screening details:

Hypertensive patients, male and female, age 40-80 years, eGFR > 60 ml/min, Urine Albumine < 700 mg/L

Period 1

Period 1 title	Treatment period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Spironolactone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Spironolactone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The study was a cross-over study. The study subjects received spironolactone 50 mg or placebo for two 4-week treatment periods in random order. The treatment periods were separated by a washout period lasting at least 1 week.

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

The study was a cross-over study. The study subjects received spironolactone 50 mg or placebo for two 4-week treatment periods in random order. The treatment periods were separated by a washout period lasting at least 1 week.

Number of subjects in period 1	Spironolactone	Placebo
Started	8	8
Completed	5	5
Not completed	3	3
Covid-19 pandemic	3	2
Malignancy suspicion	-	1

Period 2	
Period 2 title	Treatment period 2
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Spironolactone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Spironolactone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The study was a cross-over study. The study subjects received spironolactone 50 mg or placebo for two 4-week treatment periods in random order. The treatment periods were separated by a washout period lasting at least 1 week.

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

The study was a cross-over study. The study subjects received spironolactone 50 mg or placebo for two 4-week treatment periods in random order. The treatment periods were separated by a washout period lasting at least 1 week.

Notes:

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

Justification: The study is a cross-over study. Only data from the 10 subjects who completed both treatment periods are analyzed. Baseline characteristics includes the ten completing subjects.

Number of subjects in period 2[2]	Spironolactone	Placebo
Started	5	5
Completed	5	5

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: The study is a cross-over study. Only data from the 10 subjtects who completed both treatment periods are analyzed. Baseline characteristics includes the ten completing subjects.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period 2

Reporting group description: -

Reporting group values	Treatment period 2	Total	
Number of subjects	10	10	
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)	5	5	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	7	7	

End points

End points reporting groups

Reporting group title	Spironolactone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Spironolactone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Rubidium-82 clearance

End point title	Rubidium-82 clearance[1]
End point description:	
The end point is reported for both treatment periods	
End point type	Primary
End point timeframe:	
End of study	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is presented as mean +/- standard deviation

End point values	Spironolactone	Placebo	Spironolactone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: ml/min/1.73 m2				
arithmetic mean (standard deviation)	421 (± 94)	453 (± 136)	418 (± 120)	439 (± 96)

Statistical analyses

No statistical analyses for this end point

Secondary: MAG-3 clearance

End point title	MAG-3 clearance
End point description:	
The end point is reported for both treatment periods	
End point type	Secondary
End point timeframe:	
End of study	

End point values	Spironolactone	Placebo	Spironolactone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: ml/min/1.73 m2				
arithmetic mean (standard deviation)	208 (± 46)	210 (± 40)	203 (± 25)	221 (± 65)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From day 1 in teatment period 1 until 1 week after the end of treatment period 2

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Headache	Additional description: Admitted with neckpain, headache, vomiting. Blood pressure is high at admissiontime. Paracetamol relieves pain and blood pressure falls spontaneously		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transitory ischemic attack	Additional description: Admitted due to visionloss on one eye lasting 5 minutes. CT cerebrum and CT angiograhy of arteries in neck without infarction and stenosis respectively.		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Bile duct/pancreatic disease	Additional description: Admitted with fever, jaundice, pruritus. Conclusion of examinations: possible malignancy in the pancreas		
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 16 (62.50%)		
Vascular disorders			
Superficial thrombophlebitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	6		
Gastrointestinal disorders			
Loose stools	Additional description: Loose stools in a short period during the study		
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Vomiting and nausea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			
Finding of renal cyst on PET/CT			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Infections and infestations			
Fungus in groin			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Dental infection			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 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