Clinical trial results:
Treatment of congenital nephrogenic diabetes insipidus with a guanylate cyclase stimulator, riociguat or a phosphodiesterase type 5 inhibitor, sildenafil

Summary

EudraCT number	2016-001591-30
Trial protocol	DK
Global end of trial date	06 June 2019

Results information

Result version number	v1 (current)
This version publication date	04 June 2020
First version publication date	04 June 2020

Trial information

Trial identification

Sponsor protocol code	S-20150201

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Claus Bistrup
Sponsor organisation address	J.B. Winsløws Vej 4, Odense C, Denmark, 5000
Public contact	Dept. of Nephrology, Odense University Hospital, 45 65411106, ode.y@rsyd.dk
Scientific contact	Dept. of Nephrology, Odense University Hospital, 45 65411106, ode.y@rsyd.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	01 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 June 2019
Global end of trial reached?	Yes
Global end of trial date	06 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to test the hypothesis that treatment with riociguat or sildenafil in patients with NDI
caused by AVP2R mutation improves the symptoms by reducing diuresis

Protection of trial subjects:

Patients were hospitalized for the first two days of each intervention to enable close monitoring of side-effects. For the rest of each intervention, patients had daily check-ups where symptoms and side-effects were monitored and handled.

Background therapy:

None

Evidence for comparator:

Not applicable.
The effect of the two interventions was evaluated by comparing baseline values to similar values after each intervention.

Actual start date of recruitment	20 February 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: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	2

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The two subjects were included on the 20th of February 2019 after oral and written information. Written informed consent was obtained before any study related procedures.

Pre-assignment

Screening details:

The two subjects fulfilling the elegibility criteria were recruited from the outpatient clinic at the Department of Nephrology, Odense University Hospital.

Period 1

Period 1 title	Sildenafil
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Sildenafil

Arm description:

Intervention

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

Dosage and administration details:

50 mg x 3/day for 7 days

Number of subjects in period 1	Sildenafil
Started	2
Completed	2

Period 2

Period 2 title	Riociguat
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Riociguat
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Riociguat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg 3 times per day

Number of subjects in period 2	Riociguat
Started	2
Completed	2

Baseline characteristics

Reporting groups

Reporting group title	Sildenafil

Reporting group description: -

Reporting group values	Sildenafil	Total	
Number of subjects	2	2	
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)	2	2	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	28		
full range (min-max)	28 to 28	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	2	2	
Bodyweight Units: kg			
arithmetic mean	143.5		
full range (min-max)	142.4 to 144.6	-	
Height Units: cm			
arithmetic mean	182.5		
full range (min-max)	182.5 to 182.5	-	

End points

End points reporting groups

Reporting group title	Sildenafil
Reporting group description: Intervention	
Reporting group title	Riociguat
Reporting group description: -	

Primary: Diureses per hour

End point title	Diureses per hour[1]
End point description:	
End point type	Primary
End point timeframe: During water deprivation test	

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: N=2, therefor, no statistic analysis has been performed

End point values	Sildenafil	Riociguat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: mL				
arithmetic mean (full range (min-max))	1103.67 (809 to 1685)	971 (764 to 1335)		

Statistical analyses

No statistical analyses for this end point

Primary: water intake

End point title	water intake[2]
End point description:	
End point type	Primary
End point timeframe: During intervention periode	

Notes:

[2] - 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: Water intake was not measured. No statistical analysis performed.

End point values	Sildenafil	Riociguat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[3]	2[4]		
Units: mL				
arithmetic mean (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Notes:

[3] - Not measured

[4] - Not measured

Statistical analyses

No statistical analyses for this end point

Post-hoc: Diureses per 24h

End point title	Diureses per 24h

End point description:

End point type	Post-hoc

End point timeframe:

During intervention periode

End point values	Sildenafil	Riociguat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: mL				
arithmetic mean (full range (min-max))	10817.33 (8480 to 13320)	13177.83 (9240 to 18140)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Urinary osmolality

End point title	Urinary osmolality

End point description:

End point type	Post-hoc

End point timeframe:

During intervention period

End point values	Sildenafil	Riociguat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: mosm/kg				
arithmetic mean (full range (min-max))	92.58 (84 to 99)	88.08 (75 to 98)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During interventions	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	2019AB

Reporting groups	
Reporting group title	Sildnafil
Reporting group description: -	
Reporting group title	Riociguat
Reporting group description: -	

Serious adverse events	Sildnafil	Riociguat	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Sildnafil	Riociguat	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	
occurrences (all)	2	2	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	
occurrences (all)	3	1	

Abdominal discomfort	Additional description: Lower abdomen		
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Slight		
subjects affected / exposed	2 / 2 (100.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Only two participants

Notes: