

**Clinical trial results:****A Multicentre, Randomised, Open-label, Parallel-Group Pilot Study to Evaluate the Efficacy of Patiromer in Optimising Mineralocorticoid Receptor Antagonist Therapy in Heart Failure Subjects with Hyperkalaemia****Summary**

EudraCT number	2017-003555-35
Trial protocol	DE
Global end of trial date	09 October 2019

Results information

Result version number	v1 (current)
This version publication date	09 October 2020
First version publication date	09 October 2020

Trial information**Trial identification**

Sponsor protocol code	PAT-DEU-402
-----------------------	-------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fresenius Medical Care Nephrologica Deutschland GmbH
Sponsor organisation address	Else-Kröner-Strasse 1, Bad Homburg, Germany, D-61352
Public contact	Dr. John Golden, Medical Director, Fresenius Medical Care Nephrologica Deutschland GmbH, +49 6172 886 70-0, john.golden@viforpharma.com
Scientific contact	Julian V. Platon, MD, PhD Clinical Research Cardio-Renal & Orphan Hematology, Director, Vifor Pharma Management Ltd., +41 58 851 80 00, julian.platon@viforpharma.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	22 June 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 October 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of patiomer in optimising mineralocorticoid receptor antagonist (MRA) therapy in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects

Protection of trial subjects:

The study was conducted according to the principles of the World Medical Association's Declaration of Helsinki (as amended by the 64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013), and the International Council for Harmonisation (ICH) guidelines for Good Clinical Practice. Fresenius Medical Care Nephrologica Deutschland GmbH ensured that the study complied with all local, federal, or country regulatory requirements.

Background therapy:

Subjects were on:

- MRA therapy in accordance with the respective product label: eplerenone or spironolactone. Eplerenone/spironolactone target dose was 50 mg/day for both treatment groups. All subjects continued with their current eplerenone/spironolactone dose on Day 1 (when starting the study treatment). Dose adjustments could be performed starting at Visit Day 3.
- Guideline recommended heart failure (HF) therapy, i.e., on 1 or more HF therapies (e.g., angiotensin-converting enzyme inhibitor [ACEi], angiotensin receptor blocker [ARB], angiotensin receptor neprilysin inhibitor [ARNi], beta blocker [BB], diuretic) that are anticipated to remain stable during study participation with the exception of the diuretic

Evidence for comparator: -

Actual start date of recruitment	18 April 2018
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	Germany: 21
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	4
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The purpose of the screening period was to ensure that all subjects to be randomised were properly evaluated and met all study eligibility criteria. The screening period (up to 14 days) could include 2 visits (S1 and S2).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Veltassa® (patiromer)

Arm description:

To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with patiromer (8.4 g/day, titration according to label)

Arm type	Experimental
Investigational medicinal product name	Patiromer sorbitex calcium
Investigational medicinal product code	
Other name	Veltassa®
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Strength: 8.4 g/sachet

The starting dose of patiromer was 8.4 g/day orally. Dose adjustments were performed starting at Visit Day 7. Based upon the patiromer treatment algorithm, patiromer was increased in increments of 8.4 g/day if sK⁺ was ≥5.1 mmol/l (measured by local laboratory) in intervals of at least 1 week up to a maximum dose of 25.2 g/day. Doses of patiromer were in 1, 2, and 3 sachets (maximum dose).

For subjects with K⁺ <4.0 mmol/l, patiromer dose was decreased by at least 8.4 g/day. If K⁺ was <3.5 mmol/l, patiromer dose was stopped (0 g/day) and restarted at the next lowest dose once K⁺ was >4.0 mmol/l. The minimum dose of patiromer was 0 g/day

Arm title	Standard of Care
------------------	------------------

Arm description:

To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with Standard of Care (SOC) (diet, renal K⁺ elimination, reduction of K⁺-sparing drugs)

Arm type	Standard of Care
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Veltassa® (patiomer)	Standard of Care
Started	10	11
Completed	10	11

Baseline characteristics

Reporting groups

Reporting group title	Veltassa® (patiromer)
-----------------------	-----------------------

Reporting group description:

To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with patiromer (8.4 g/day, titration according to label)

Reporting group title	Standard of Care
-----------------------	------------------

Reporting group description:

To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with Standard of Care (SOC) (diet, renal K⁺ elimination, reduction of K⁺-sparing drugs)

Reporting group values	Veltassa® (patiromer)	Standard of Care	Total
Number of subjects	10	11	21
Age categorical			
Units: Subjects			
Adults (18-64 years)	2	2	4
From 65-84 years	8	9	17
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	70.8	72.8	-
standard deviation	± 8.84	± 7.49	-
Gender categorical			
Units: Subjects			
Female	1	1	2
Male	9	10	19
MRA treatment			
MRA = Mineralocorticoid receptor antagonist			
Units: Subjects			
Eplerenone	4	5	9
Spironolactone	6	6	12
Serum potassium			
Units: Subjects			
<5.1 mmol/l	0	0	0
≥5.1-<5.5 mmol/l	3	3	6
≥5.5 mmol/l	7	8	15

End points

End points reporting groups

Reporting group title	Veltassa® (patiomer)
Reporting group description:	To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with patiomer (8.4 g/day, titration according to label)
Reporting group title	Standard of Care
Reporting group description:	To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with Standard of Care (SOC) (diet, renal K+ elimination, reduction of K+-sparing drugs)

Primary: Subjects maintaining or achieving MRA target dose at Day 42

End point title	Subjects maintaining or achieving MRA target dose at Day 42 ^[1]
End point description:	MRA target dose: guideline recommended and evidence-based target dose of 50 mg/day eplerenone or spironolactone
End point type	Primary
End point timeframe:	Day 42

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: Odds ratio estimate with its exact 95% confidence interval (CI) was planned to be presented. However, due to the early study termination and limited data available for the primary efficacy endpoint, the corresponding odds ratio could not be computed.

End point values	Veltassa® (patiomer)	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: Subjects	5	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Assessment (PGA)

End point title	Patient Global Assessment (PGA)
End point description:	The PGA allowed the subject to assess his/her medical condition at Visit Day 21 and Visit Day 42
Question to the subject:	'Since I started my participation in this study, my medical condition:...'
End point type	Secondary
End point timeframe:	From Baseline to Day 21 and Day 42

End point values	Veltassa® (patiromer)	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: Subjects				
Day 21 - Has much improved	0	0		
Day 21 - Has (moderately) improved	3	2		
Day 21 - Has a little improved	3	2		
Day 21 - Is unchanged	3	7		
Day 21 - Is a little worse	0	0		
Day 21 - Is (moderately) worse	1	0		
Day 21 - Is much worse	0	0		
Day 42 - Has much improved	2	0		
Day 42 - Has (moderately) improved	3	2		
Day 42 - Has a little improved	3	2		
Day 42 - Is unchanged	2	6		
Day 42 - Is a little worse	0	0		
Day 42 - Is (moderately) worse	0	0		
Day 42 - Is much worse	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in EQ-5D-5L Questionnaire

End point title	Change in EQ-5D-5L Questionnaire
-----------------	----------------------------------

End point description:

EQ-5D-5L: European Quality of Life 5-Dimensions 5-Level

The EQ-5D-5L index value using the German Value Set ranges from -0.661 (worst health state) to 1 (best health state).

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

End point timeframe:

From Baseline to Day 21 and Day 42

End point values	Veltassa® (patiromer)	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: Index Value				
arithmetic mean (standard deviation)				
Day 21	-0.051 (± 0.1266)	-0.015 (± 0.1319)		
Day 42	-0.036 (± 0.0589)	-0.015 (± 0.1279)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in NYHA class

End point title | Change in NYHA class

End point description:

NYHA: New York Heart Association

End point type | Secondary

End point timeframe:

From Baseline to Day 21 and Day 42

End point values	Veltassa® (patiromer)	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: Subjects				
Day 21 - Better	3	2		
Day 21 - No Change	4	9		
Day 21 - Worse	3	0		
Day 42 - Better	4	3		
Day 42 - No Change	3	8		
Day 42 - Worse	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in functional capacity

End point title | Change in functional capacity

End point description:

SPPB - Short Physical Performance Battery

The SPPB measured balance, gait speed, and lower limb strength and endurance (chair stand test). The SPPB Protocol Total Score ranges from 0 points (least performance) to 12 points (best performance).

End point type | Secondary

End point timeframe:

From Baseline to Day 21 and Day 42

End point values	Veltassa® (patiromer)	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: SPPB Total Score				
arithmetic mean (standard deviation)				
Day 21	-0.4 (± 1.58)	0.5 (± 1.35)		
Day 42	0.0 (± 2.11)	0.5 (± 1.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in eplerenone or spironolactone dosage

End point title	Change in eplerenone or spironolactone dosage
End point description:	
End point type	Secondary
End point timeframe:	
From Baseline to Follow up visit	

End point values	Veltassa® (patiromer)	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: mg/day				
arithmetic mean (standard deviation)				
Day 3	-1.250 (± 3.9528)	-4.167 (± 10.2062)		
Day 7	-2.500 (± 7.9057)	-8.333 (± 10.2062)		
Day 14	1.250 (± 14.9652)	-5.357 (± 9.8349)		
Day 21	5.000 (± 10.5409)	-5.000 (± 6.8465)		
Day 28	3.750 (± 11.8585)	-8.333 (± 10.2062)		
Day 42	8.333 (± 12.5000)	-10.417 (± 9.4097)		
Follow up	2.778 (± 15.0231)	-10.000 (± 16.2980)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to Follow up visit (Day 49)

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20.1
--------------------	------

Reporting groups

Reporting group title	Veltassa® (patiromer)
-----------------------	-----------------------

Reporting group description:

To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with patiromer (8.4 g/day, titration according to label)

Reporting group title	Standard of Care
-----------------------	------------------

Reporting group description:

To manage hyperkalaemia in hyperkalaemic heart failure with reduced ejection fraction (HFrEF) subjects treated with eplerenone or spironolactone with Standard of Care (SOC) (diet, renal K+ elimination, reduction of K+-sparing drugs)

Serious adverse events	Veltassa® (patiromer)	Standard of Care	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood potassium increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Veltassa® (patiromer)	Standard of Care	
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 10 (80.00%)	6 / 11 (54.55%)	
Investigations			
Blood creatine increased subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cardioactive drug level increased subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Blood potassium increased subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vascular disorders			
Peripheral arterial occlusive disease subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue subjects affected / exposed	2 / 10 (20.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Nausea subjects affected / exposed	3 / 10 (30.00%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Constipation subjects affected / exposed	2 / 10 (20.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Diarrhoea subjects affected / exposed	2 / 10 (20.00%)	1 / 11 (9.09%)	
occurrences (all)	3	1	
Eructation subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) Renal failure subjects affected / exposed occurrences (all) Renal impairment subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0	0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Osteitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1 1 / 10 (10.00%) 1	0 / 11 (0.00%) 0 0 / 11 (0.00%) 0	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Gastrointestinal infection	3 / 10 (30.00%) 3 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1	

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 11 (9.09%) 1	
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2017	Version 2.0/Amendment 1 - Changes requested from Ethics committee and BfArM; addition of exclusion criteria; source of pregnancy test; various administrative edits.
06 February 2018	Version 3.0/Amendment 2 - Addition to prohibited therapy; clarification to urine parameters; RAC introduction; updated appendices; various administrative edits.
20 August 2018	Version 4.0/Amendment 3 - Clarification of target number of patients; initial treatment day change; change in inclusion and exclusion criteria; removal of certain prohibited medications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported