Clinical trial results:
A Multicenter, Open-Label, Single-Arm Study to Evaluate a Titration Regimen for RLY5016 in Heart Failure Patients with Chronic Kidney Disease

Summary

EudraCT number	2010-018838-45
Trial protocol	SI
Global end of trial date	23 September 2010

Results information

Result version number	v1 (current)
This version publication date	06 August 2016
First version publication date	06 August 2016

Trial information

Trial identification

Sponsor protocol code	RLY5016–204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01130597
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Relypsa, Inc.
Sponsor organisation address	100 Cardinal Way, Redwood City, United States, 94063
Public contact	Medical Information, Relypsa, Inc., medinfo@relypsa.com
Scientific contact	Medical Information, Relypsa, Inc., medinfo@relypsa.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	23 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2010
Global end of trial reached?	Yes
Global end of trial date	23 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the feasibility of individualized titration of patiromer according to serum potassium. This study also assessed the safety and tolerability of patiromer and the effects of patiromer on serum potassium in heart failure (HF) participants with chronic kidney disease (CKD).

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2010
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	Georgia: 45
Country: Number of subjects enrolled	Slovenia: 18
Worldwide total number of subjects	63
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)	17
From 65 to 84 years	43
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible participants were ≥ 18 years old, had a history of chronic HF, were clinically indicated to initiate spironolactone therapy, had a serum potassium measurement of 4.3 – 5.1 mEq/L at screening and baseline, had CKD (eGFR < 60 mL/min/1.73 m2 at screening), and were taking one or more HF therapies (ACEIs, ARBs, or BBs).

Period 1

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

Arms

Arm title	Patiromer

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Patiromer
Investigational medicinal product code	
Other name	RLY5016 for Oral Suspension
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patiromer, 10 g, orally, twice a day for up to 56 days

Investigational medicinal product name	Spironolactone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Spironolactone, starting dose of 25 mg, orally, once a day. At clinic visits starting on Day 7 through Day 49, the dose could be increased once to a maximum of 50 mg/day based on local laboratory serum potassium values; spironolactone dose reductions were not allowed.

Number of subjects in period 1	Patiromer
Started	63
Completed	56
Not completed	7
Adverse event, serious fatal	1
Adverse event, non-fatal	4
Protocol-specified (High K+)	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Patiromer

Reporting group description: -

Reporting group values	Patiromer	Total	
Number of subjects	63	63	
Age categorical Units: Subjects			
Adults (18-64 years)	17	17	
From 65-84 years	43	43	
85 years and over	3	3	
Age continuous Units: years			
arithmetic mean	70.8		
full range (min-max)	53 to 86	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	39	39	

End points

End points reporting groups

Reporting group title	Patiromer

Reporting group description: -

Primary: Percentage of Participants With Serum Potassium in the Range of 3.5 - 5.5 mEq/L at the End of Treatment

End point title	Percentage of Participants With Serum Potassium in the Range of 3.5 - 5.5 mEq/L at the End of Treatment[1]

End point description:

End point type	Primary

End point timeframe:

56 Days

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: Because this is a one arm study, the database displayed an error upon validation, prompting for a selection of two arms instead of one. Therefore, the Statistical Analysis was entered as a 95% confidence interval proceeding the outcome data. Clopper-Pearson was used to arrive at this value.

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63[2]			
Units: percentage of participants				
number (confidence interval 95%)	90.5 (80.4 to 96.4)			

Notes:

[2] - Clopper-Pearson was used to arrive at the 95% Confidence Interval

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serum Potassium in the Range of 3.5 - 5.5 mEq/L at Week 4

End point title	Percentage of Participants With Serum Potassium in the Range of 3.5 - 5.5 mEq/L at Week 4

End point description:

End point type	Secondary

End point timeframe:

28 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	61[3]			
Units: percentage of participants				
number (not applicable)	96.7			

Notes:

[3] - Participants with available data at Week 4.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serum Potassium in the Range of 3.5 - 5.5 mEq/L at Week 8

End point title	Percentage of Participants With Serum Potassium in the Range of 3.5 - 5.5 mEq/L at Week 8

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	57[4]			
Units: percentage of participants				
number (not applicable)	93			

Notes:

[4] - Participants with available data at Week 8.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serum Potassium in the Range of 4.0 - 5.1 mEq/L at Week 4

End point title	Percentage of Participants With Serum Potassium in the Range of 4.0 - 5.1 mEq/L at Week 4

End point description:

End point type	Secondary

End point timeframe:

28 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	61[5]			
Units: percentage of participants				
number (not applicable)	78.7			

Notes:

[5] - Participants with available data at Week 4.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serum Potassium in the Range of 4.0 - 5.1 mEq/L at Week 8

End point title	Percentage of Participants With Serum Potassium in the Range of 4.0 - 5.1 mEq/L at Week 8

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	57[6]			
Units: percentage of participants				
number (not applicable)	86			

Notes:

[6] - Participants with available data at Week 8.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serum Potassium in the Range of 4.0 - 5.1 mEq/L at the End of Treatment

End point title	Percentage of Participants With Serum Potassium in the Range of 4.0 - 5.1 mEq/L at the End of Treatment

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63[7]			
Units: percentage of participants				
number (confidence interval 95%)	84.1 (72.1 to 92.1)			

Notes:

[7] - Clopper-Pearson was used to arrive at the 95% Confidence Interval

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Dose of Patiromer at End of Treatment

End point title	Mean Dose of Patiromer at End of Treatment

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: gram(s)				
arithmetic mean (standard deviation)	22.5 (± 7.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Requiring Patiromer Uptitration

End point title	Percentage of Participants Requiring Patiromer Uptitration

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percentage of participants				
number (not applicable)	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Requiring Patiromer Downtitration

End point title	Percentage of Participants Requiring Patiromer Downtitration

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percentage of participants				
number (not applicable)	12.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to First Patiromer Dose Titration

End point title	Median Time to First Patiromer Dose Titration

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: day				
median (confidence interval 95%)	21 (14 to 36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of Patiromer Titrations

End point title	Mean Number of Patiromer Titrations

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: patiromer titrations				
arithmetic mean (standard deviation)	1.3 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Patiromer Dose at Week 1

End point title	Mean Patiromer Dose at Week 1

End point description:

End point type	Secondary

End point timeframe:

Up to Week 1

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: gram(s)				
arithmetic mean (standard deviation)	20 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Patiromer Dose at Week 4

End point title	Mean Patiromer Dose at Week 4

End point description:

End point type	Secondary

End point timeframe:

Up to Week 4

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: gram(s)				
arithmetic mean (standard deviation)	21.9 (± 8.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Patiromer Dose at Week 8

End point title	Mean Patiromer Dose at Week 8

End point description:

End point type	Secondary

End point timeframe:

Up to Week 8

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: gram(s)				
arithmetic mean (standard deviation)	23 (± 12.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Serum Potassium to End of Treatment

End point title	Mean Change From Baseline in Serum Potassium to End of Treatment

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: milliequivalent(s)/litre				
arithmetic mean (standard deviation)	-0.13 (± 0.686)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Discontinuing Due to Hyperkalemia (Serum Potassium > 5.5 mEq/L)

End point title	Percentage of Participants Discontinuing Due to Hyperkalemia (Serum Potassium > 5.5 mEq/L)

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percentage of participants				
number (not applicable)	1.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Whose Spironolactone Dose Was Increased Up to 50 mg/Day

End point title	Percentage of Patients Whose Spironolactone Dose Was Increased Up to 50 mg/Day

End point description:

End point type	Secondary

End point timeframe:

56 Days

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: percentage of participants				
number (not applicable)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Urine Albumin to Creatinine Ratio (ACR) From Baseline to Week 4 Among Participants With ACR ≥ 30 mg/g at Baseline

End point title	Change in Urine Albumin to Creatinine Ratio (ACR) From Baseline to Week 4 Among Participants With ACR ≥ 30 mg/g at Baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline and Day 28

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	31[8]			
Units: mg/g				
arithmetic mean (standard error)	-291.01 (± 130.7973)			

Notes:

[8] - Participants with urine ACR ≥ 30 mg/g at baseline and available data at Week 4

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ACR From Baseline to Week 8 Among Participants With Urine ACR ≥ 30 mg/g at Baseline

End point title	Change in ACR From Baseline to Week 8 Among Participants With Urine ACR ≥ 30 mg/g at Baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline and Day 56

End point values	Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	30[9]			
Units: mg/g				
arithmetic mean (standard error)	-291.06 (± 141.5644)			

Notes:

[9] - Participants with urine ACR ≥ 30 mg/g at baseline and available data at Week 8

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 7 days after Day 56 or last patiromer dose, whichever was earlier.

Adverse event reporting additional description:

Participants who received at least one dose of trial medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Patiromer

Reporting group description: -

Serious adverse events	Patiromer		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 63 (9.52%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sudden death	Additional description: Sudden death occurred during the follow up period, after completing the study.		
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Azotaemia			

subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	3 / 63 (4.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal abscess			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 63 (1.59%)		
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	Patiromer		
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 63 (6.35%)		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 5		

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