



Clinical trial results:

A Multicenter, Randomized, Open-Label, Dose Ranging Study to Evaluate the Efficacy and Safety of RLY5016 in the Treatment of Hyperkalemia in Patients with Hypertension and Diabetic Nephropathy Receiving ACEI and/or ARB Drugs, with or without Spironolactone Summary

EudraCT number	2011-000165-12
Trial protocol	HU DE AT SI
Global end of trial date	17 June 2013

Results information

Result version number	v1 (current)
This version publication date	11 August 2016
First version publication date	11 August 2016

Trial information

Trial identification

Sponsor protocol code	RLY5016-205
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01371747
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	10 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 June 2013
Global end of trial reached?	Yes
Global end of trial date	17 June 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the optimal starting dose of RLY5016 in treating hyperkalemia in patients with hypertension and diabetic nephropathy receiving ACEI and/or ARB drugs, with or without spironolactone

Protection of trial subjects:

This study was conducted in conformance 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:

All subjects were on ACEI and/or ARB drugs with or without spironolactone.

Evidence for comparator: -

Actual start date of recruitment	16 May 2011
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	Hungary: 50
Country: Number of subjects enrolled	Georgia: 181
Country: Number of subjects enrolled	Croatia: 24
Country: Number of subjects enrolled	Serbia: 36
Country: Number of subjects enrolled	Slovenia: 15
Worldwide total number of subjects	306
EEA total number of subjects	89

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)	123
From 65 to 84 years	183
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening serum potassium ≤ 5 mEq/L (milliequivalent) entered Run-in: Cohort 1 stopped ACEI/ARB (angiotensin-converting enzyme inhibitor/angiotensin receptor blockers), started losartan; Cohort 2 started spironolactone; Run-in (Cohorts 1 and 2) or screening (Cohort 3) > 5 mEq/L entered study.

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	Stratum 1: 8.4 g/d patiromer

Arm description:

Participants with baseline serum potassium $> 5.0 - 5.5$ mEq/L randomized to 8.4 g/day patiromer starting dose, orally, as a divided dose twice a day.

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:

Participants with baseline serum potassium $> 5.0 - 5.5$ mEq/L randomized to 8.4 g/day patiromer starting dose, orally, as a divided dose twice a day.

Arm title	Stratum 1: 16.8 g/d Patiromer
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Arm description:

Participants with baseline serum potassium $> 5.0 - 5.5$ mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.

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:

Participants with baseline serum potassium $> 5.0 - 5.5$ mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.

Arm title	Stratum 1: 25.2 g/d Patiromer
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Arm description:

Participants with baseline serum potassium $> 5.0 - 5.5$ mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.

Arm type	Experimental
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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:

Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.

Arm title	Stratum 2: 16.8 g/d Patiromer
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Arm description:

Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.

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:

Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.

Arm title	Stratum 2: 25.2 g/d Patiromer
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Arm description:

Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.

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:

Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.

Arm title	Stratum 2: 33.6 g/d Patiromer
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Arm description:

Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 33.6 g/day patiromer starting dose, orally, as a divided dose twice a day.

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:

Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 33.6 g/day patiromer starting dose, orally, as a divided dose twice a day.

Number of subjects in period 1^[1]	Stratum 1: 8.4 g/d patiomer	Stratum 1: 16.8 g/d Patiomer	Stratum 1: 25.2 g/d Patiomer
Started	74	73	73
Completed	56	51	50
Not completed	18	22	23
Adverse event, serious fatal	1	-	4
Non-Compliance	3	4	3
Consent withdrawn by subject	6	11	5
Physician decision	-	-	-
Low Serum Potassium Results	1	1	1
Adverse event, non-fatal	4	2	7
Other Reasons	2	1	1
High Serum Potassium Results	1	1	1
Abnormal Renal Function	-	2	-
Protocol deviation	-	-	1

Number of subjects in period 1^[1]	Stratum 2: 16.8 g/d Patiomer	Stratum 2: 25.2 g/d Patiomer	Stratum 2: 33.6 g/d Patiomer
Started	26	28	30
Completed	17	21	16
Not completed	9	7	14
Adverse event, serious fatal	1	2	-
Non-Compliance	-	-	1
Consent withdrawn by subject	2	2	4
Physician decision	-	1	-
Low Serum Potassium Results	1	-	3
Adverse event, non-fatal	2	2	2
Other Reasons	-	-	1
High Serum Potassium Results	2	-	2
Abnormal Renal Function	1	-	1
Protocol deviation	-	-	-

Notes:

[1] - 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: 306 participants were randomized and stratified by baseline serum potassium (2 randomized participants in Stratum 1 did not receive any study drug; 1 participant withdrew consent and 1 participant was randomized in error and was withdrawn from the study); 304 participants were analyzed for safety.

Baseline characteristics

Reporting groups

Reporting group title	Stratum 1: 8.4 g/d patiromer
Reporting group description: Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 8.4 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 1: 16.8 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 1: 25.2 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 2: 16.8 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 2: 25.2 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 2: 33.6 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 33.6 g/day patiromer starting dose, orally, as a divided dose twice a day.	

Reporting group values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer
Number of subjects	74	73	73
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	29	28
From 65-84 years	46	44	45
85 years and over	0	0	0
Age continuous Units: years			
median	67	70	68
full range (min-max)	46 to 80	37 to 79	40 to 79
Gender categorical Units: Subjects			
Female	29	26	26
Male	45	47	47

Reporting group values	Stratum 2: 16.8 g/d Patiomer	Stratum 2: 25.2 g/d Patiomer	Stratum 2: 33.6 g/d Patiomer
Number of subjects	26	28	30
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	12	13
From 65-84 years	14	16	17
85 years and over	0	0	0
Age continuous Units: years			
median	66.5	68.5	65
full range (min-max)	56 to 76	39 to 80	44 to 78
Gender categorical Units: Subjects			
Female	8	13	10
Male	18	15	20

Reporting group values	Total		
Number of subjects	304		
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)	122		
From 65-84 years	182		
85 years and over	0		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	112		
Male	192		

End points

End points reporting groups

Reporting group title	Stratum 1: 8.4 g/d patiromer
Reporting group description: Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 8.4 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 1: 16.8 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 1: 25.2 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.0 - 5.5 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 2: 16.8 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 16.8 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 2: 25.2 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 25.2 g/day patiromer starting dose, orally, as a divided dose twice a day.	
Reporting group title	Stratum 2: 33.6 g/d Patiromer
Reporting group description: Participants with baseline serum potassium > 5.5 to < 6.0 mEq/L randomized to 33.6 g/day patiromer starting dose, orally, as a divided dose twice a day.	

Primary: Least Squares Mean Change in Serum Potassium From Baseline to Week 4 or Time of First Titration for Each Individual Starting Dose Group

End point title	Least Squares Mean Change in Serum Potassium From Baseline to Week 4 or Time of First Titration for Each Individual Starting Dose Group ^[1]
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End point description:

Least square mean changes from Baseline to Week 4/first titration were derived from parallel lines ANCOVA model with randomized starting dose and baseline serum potassium value as covariates. Individual dose group was compared to its baseline values.

End point type	Primary
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End point timeframe:

Baseline to Week 4 or First Titration which could occur at any scheduled study visit after patiromer initiation.

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: Individual dose group was compared to its baseline values. P-Value <0.001; method: ANCOVA

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	72	72	26
Units: mEq/L				
least squares mean (standard error)	-0.35 (± 0.066)	-0.51 (± 0.067)	-0.55 (± 0.067)	-0.87 (± 0.134)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	30		
Units: mEq/L				
least squares mean (standard error)	-0.97 (± 0.132)	-0.92 (± 0.125)		

Statistical analyses

No statistical analyses for this end point

Secondary: Least Squares Mean Change in Serum Potassium From Baseline to Week 8 or Time of First Titration for Each Individual Starting Dose Group

End point title	Least Squares Mean Change in Serum Potassium From Baseline to Week 8 or Time of First Titration for Each Individual Starting Dose Group
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End point description:

Least squares mean changes from Baseline to Week 8/first titration were derived from parallel lines ANCOVA model with randomized starting dose and baseline serum potassium value as covariates. Individual dose group was compared to its baseline values.

End point type	Secondary
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End point timeframe:

Baseline to Week 8 or First Titration which could occur at any scheduled study visit after patiromer initiation.

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	72	72	26
Units: mEq/L				
least squares mean (standard error)	-0.35 (± 0.07)	-0.47 (± 0.07)	-0.54 (± 0.07)	-0.88 (± 0.142)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	30		
Units: mEq/L				
least squares mean (standard error)	-0.95 (± 0.139)	-0.91 (± 0.132)		

Statistical analyses

No statistical analyses for this end point

Secondary: Least Squares Mean Change in Serum Potassium From Baseline to Day 3 During the Treatment Initiation Period for Each Individual Starting Dose Group

End point title	Least Squares Mean Change in Serum Potassium From Baseline to Day 3 During the Treatment Initiation Period for Each Individual Starting Dose Group
End point description:	Least squares mean changes from Baseline to Day 3 were derived from parallel lines ANCOVA model with randomized starting dose and baseline serum potassium value as covariates. Individual dose group was compared to its baseline values.
End point type	Secondary
End point timeframe:	Baseline to Day 3

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	63	69	25
Units: mEq/L				
least squares mean (standard error)	-0.26 (± 0.048)	-0.28 (± 0.05)	-0.31 (± 0.047)	-0.65 (± 0.086)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	30		
Units: mEq/L				
least squares mean (standard error)	-0.59 (± 0.084)	-0.53 (± 0.079)		

Statistical analyses

Secondary: Mean Change in Serum Potassium From Baseline to Week 52 During the Long-term Maintenance Period for Each Individual Starting Dose Group

End point title	Mean Change in Serum Potassium From Baseline to Week 52 During the Long-term Maintenance Period for Each Individual Starting Dose Group
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End point description:

Mean Change in Serum Potassium From Baseline to Week 52 During the Long-term Maintenance Period for Each Individual Starting Dose Group. Individual dose group was compared to its baseline values.

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	49	44	15
Units: mEq/L				
arithmetic mean (standard deviation)	-0.54 (± 0.465)	-0.44 (± 0.44)	-0.5 (± 0.417)	-1 (± 0.466)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: mEq/L				
arithmetic mean (standard deviation)	-0.96 (± 0.414)	-1.17 (± 0.569)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in Serum Potassium From Week 52 or Last Patiromer Dose (if Occurred Before Week 52) to Follow-up Visits Plus 7 Days

End point title	Mean Change in Serum Potassium From Week 52 or Last Patiromer Dose (if Occurred Before Week 52) to Follow-up Visits Plus 7 Days
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End point description:

Mean Change in Serum Potassium From Week 52 or Last Patiromer Dose (if Occurred Before Week 52) to Follow-up Visits Plus 7 Days. Individual dose group was compared to its baseline values.

End point type	Secondary
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End point timeframe:

Week 52 or Last Patiromer Dose (if Occurred before Week 52) to Following up Visit Plus 7 Days

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	50	20
Units: mEq/L				
arithmetic mean (standard deviation)	0.36 (± 0.567)	0.22 (± 0.424)	0.3 (± 0.508)	0.41 (± 0.66)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	20		
Units: mEq/L				
arithmetic mean (standard deviation)	0.39 (± 0.331)	0.58 (± 0.557)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Achieving Serum Potassium Levels Within 3.5 to 5.5 mEq/L at Week 8 for Each Individual Starting Dose Group

End point title	Proportion of Participants Achieving Serum Potassium Levels Within 3.5 to 5.5 mEq/L at Week 8 for Each Individual Starting Dose Group
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End point description:

Proportion of Participants Achieving Serum Potassium Levels Within 3.5 to 5.5 mEq/L at Week 8 for Each Individual Starting Dose Group

End point type	Secondary
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End point timeframe:

Baseline to Week 8

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	65	64	24
Units: Percentage of participants				
number (confidence interval 95%)	100 (94.3 to 100)	100 (94.5 to 100)	98.4 (91.6 to 100)	91.7 (73 to 99)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: Percentage of participants				
number (confidence interval 95%)	95.8 (78.9 to 99.9)	95.5 (77.2 to 99.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Serum Potassium Measurement of 4.0 - 5.0 mEq/L During Treatment Initiation Period for Each Individual Starting Dose Group

End point title	Time to First Serum Potassium Measurement of 4.0 - 5.0 mEq/L During Treatment Initiation Period for Each Individual Starting Dose Group
End point description:	Time to First Serum Potassium Measurement of 4.0 - 5.0 mEq/L During Treatment Initiation Period for Each Individual Starting Dose Group
End point type	Secondary
End point timeframe:	Baseline to Week 8

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	72	73	26
Units: days				
median (confidence interval 95%)	4 (4 to 5)	4 (4 to 6)	4 (4 to 5)	8 (4 to 9)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: days				
median (confidence interval 95%)	7.5 (4 to 8)	8 (4 to 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportions of Participants Achieving Serum Potassium Levels Within 3.8 to 5.0 mEq/L at Week 52 for Each Individual Starting Dose Group

End point title	Proportions of Participants Achieving Serum Potassium Levels Within 3.8 to 5.0 mEq/L at Week 52 for Each Individual Starting Dose Group
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End point description:

Proportions of Participants Achieving Serum Potassium Levels Within 3.8 to 5.0 mEq/L at Week 52 for Each Individual Starting Dose Group

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	63	59	22
Units: percentage of participants				
number (confidence interval 95%)	86.3 (73.7 to 94.3)	81.6 (68 to 91.2)	88.9 (75.9 to 96.3)	86.7 (59.5 to 98.3)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: percentage of participants				
number (confidence interval 95%)	89.5 (66.9 to 98.7)	93.3 (68.1 to 99.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Achieving Serum Potassium Levels Within 4.0 to 5.0 mEq/L at Week 8 for Each Individual Starting Dose Group

End point title	Proportion of Participants Achieving Serum Potassium Levels Within 4.0 to 5.0 mEq/L at Week 8 for Each Individual Starting Dose Group
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End point description:

Proportion of Participants Achieving Serum Potassium Levels Within 4.0 to 5.0 mEq/L at Week 8 for Each Individual Starting Dose Group

End point type	Secondary
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End point timeframe:

Baseline to Week 8

End point values	Stratum 1: 8.4 g/d patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer	Stratum 2: 16.8 g/d Patiromer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	65	64	24
Units: percentage of participants				
number (confidence interval 95%)	95.2 (86.7 to 99)	90.8 (81 to 96.5)	81.3 (69.5 to 89.9)	79.2 (57.8 to 92.9)

End point values	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: percentage of participants				
number (confidence interval 95%)	91.7 (73 to 99)	77.3 (54.6 to 92.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 28 days after end of treatment or last patiromer dose, whichever was earlier.

Adverse event reporting additional description:

Randomized participants who received at least one dose of trial medication

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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Reporting groups

Reporting group title	Stratum 1: 8.4 g/d Patiromer
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Reporting group description: -

Reporting group title	Stratum 1: 16.8 g/d Patiromer
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Reporting group description: -

Reporting group title	Stratum 1: 25.2 g/d Patiromer
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Reporting group description: -

Reporting group title	Stratum 2: 16.8 g/d Patiromer
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Reporting group description: -

Reporting group title	Stratum 2: 25.2 g/d Patiromer
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Reporting group description: -

Reporting group title	Stratum 2: 33.6 g/d Patiromer
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Reporting group description: -

Serious adverse events	Stratum 1: 8.4 g/d Patiromer	Stratum 1: 16.8 g/d Patiromer	Stratum 1: 25.2 g/d Patiromer
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 74 (12.16%)	10 / 73 (13.70%)	10 / 73 (13.70%)
number of deaths (all causes)	1	2	6
number of deaths resulting from adverse events	0	0	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Diabetic vascular disorder			
subjects affected / exposed	2 / 74 (2.70%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Femoral artery occlusion			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			

subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 74 (1.35%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Brain death			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sudden cardiac death			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	3 / 73 (4.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3

Sudden death			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal and urinary disorders			
Nephropathy toxic			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			

subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			
subjects affected / exposed	0 / 74 (0.00%)	2 / 73 (2.74%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerotic gangrene			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			

subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Stratum 2: 16.8 g/d Patiromer	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 26 (23.08%)	5 / 28 (17.86%)	4 / 30 (13.33%)
number of deaths (all causes)	1	4	1
number of deaths resulting from adverse events			
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Diabetic vascular disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral artery occlusion			

subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	1 / 26 (3.85%)	1 / 28 (3.57%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Brain death			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 26 (3.85%)	2 / 28 (7.14%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1

Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephropathy toxic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			

subjects affected / exposed	1 / 26 (3.85%)	1 / 28 (3.57%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerotic gangrene			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Stratum 1: 8.4 g/d Patiomer	Stratum 1: 16.8 g/d Patiomer	Stratum 1: 25.2 g/d Patiomer
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 74 (37.84%)	29 / 73 (39.73%)	29 / 73 (39.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 74 (6.76%)	7 / 73 (9.59%)	2 / 73 (2.74%)
occurrences (all)	6	9	2
Hypotension			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	1 / 73 (1.37%)
occurrences (all)	0	1	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	2 / 73 (2.74%)
occurrences (all)	0	1	2
Cardiac failure chronic			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 73 (1.37%)
occurrences (all)	0	0	1
Ventricular extrasystoles			
subjects affected / exposed	2 / 74 (2.70%)	4 / 73 (5.48%)	2 / 73 (2.74%)
occurrences (all)	2	4	2
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 74 (4.05%)	2 / 73 (2.74%)	1 / 73 (1.37%)
occurrences (all)	3	2	1
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	2 / 73 (2.74%) 2	4 / 73 (5.48%) 4
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	6 / 74 (8.11%) 6	5 / 73 (6.85%) 7	1 / 73 (1.37%) 1
Constipation subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 6	3 / 73 (4.11%) 5	4 / 73 (5.48%) 4
Renal and urinary disorders			
Renal failure chronic subjects affected / exposed occurrences (all)	5 / 74 (6.76%) 5	4 / 73 (5.48%) 4	2 / 73 (2.74%) 2
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	3 / 74 (4.05%) 3	0 / 73 (0.00%) 0	4 / 73 (5.48%) 5
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 74 (4.05%) 6	3 / 73 (4.11%) 3	2 / 73 (2.74%) 4
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	1 / 73 (1.37%) 1	2 / 73 (2.74%) 2
Metabolism and nutrition disorders			
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	1 / 73 (1.37%) 1	1 / 73 (1.37%) 2
Hypomagnesaemia subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 4	5 / 73 (6.85%) 7	6 / 73 (8.22%) 7
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	2 / 73 (2.74%) 2	1 / 73 (1.37%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 3	1 / 73 (1.37%) 1	0 / 73 (0.00%) 0

Non-serious adverse events	Stratum 2: 16.8 g/d Patiromer	Stratum 2: 25.2 g/d Patiromer	Stratum 2: 33.6 g/d Patiromer
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 26 (53.85%)	14 / 28 (50.00%)	22 / 30 (73.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 26 (15.38%)	2 / 28 (7.14%)	4 / 30 (13.33%)
occurrences (all)	5	2	5
Hypotension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 26 (3.85%)	2 / 28 (7.14%)	0 / 30 (0.00%)
occurrences (all)	1	4	0
Cardiac failure chronic			
subjects affected / exposed	2 / 26 (7.69%)	0 / 28 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	2 / 30 (6.67%)
occurrences (all)	0	1	3
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 26 (0.00%)	0 / 28 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 28 (3.57%)	2 / 30 (6.67%)
occurrences (all)	0	1	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 26 (11.54%)	1 / 28 (3.57%)	1 / 30 (3.33%)
occurrences (all)	4	1	1
Constipation			
subjects affected / exposed	2 / 26 (7.69%)	1 / 28 (3.57%)	5 / 30 (16.67%)
occurrences (all)	3	1	5
Renal and urinary disorders			

Renal failure chronic subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	3 / 28 (10.71%) 3	6 / 30 (20.00%) 6
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 28 (3.57%) 1	0 / 30 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 28 (7.14%) 2	0 / 30 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 28 (3.57%) 1	2 / 30 (6.67%) 2
Metabolism and nutrition disorders			
Hypoglycaemia subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	1 / 28 (3.57%) 1	3 / 30 (10.00%) 5
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	4 / 28 (14.29%) 5	5 / 30 (16.67%) 5
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 28 (7.14%) 2	0 / 30 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 3	0 / 28 (0.00%) 0	3 / 30 (10.00%) 3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 June 2011	<p>Added Long-Term Maintenance Period and Long-Term Maintenance Titration Algorithm</p> <p>Added Weekly Maintenance Visits</p> <p>Added Mandatory Safety Visits (previously called Mandatory Safety Follow-up Visits)</p> <p>Added New Secondary Objective</p> <p>Increased Patient Sample Size</p> <p>Added RLY5016 Dose Group to Stratum 2</p> <p>Added New Cohort for Hyperkalemic Patients (Cohort 3)</p> <p>Revised Allocation of Patients to Cohorts</p> <p>Clarified Re-Screening Procedures, Revised Description of Run-In Period, and Added Unscheduled Visit for Cohort 1 and 2 Screening/Enrollment Failures</p> <p>Revised Eligibility Criteria (IC #7; EC #2, 3, 17)</p> <p>Revised Eligibility Criteria (IC #5)</p> <p>Revised Eligibility Criteria (IC #4)</p> <p>Revised Eligibility Criteria (IC #3, 4; EC #2, 13)</p> <p>Deleted Exclusion Criterion</p> <p>Updated Study Variables</p> <p>Revised Follow-up Period and Treatment Discontinuation</p> <p>Added Allowed Medications during the Long-Term Maintenance Period</p> <p>Clarified Allowed and Prohibited Concomitant Medications</p> <p>Updated Clinical Experience</p> <p>Updated Rationale for Study Design</p> <p>Expanded Summary of Known and Potential Benefits and Risks</p> <p>Clarified Serum Potassium Collection Procedure</p> <p>Revised Withdrawal Criteria</p> <p>Added Clarifications to Study Procedures</p> <p>Updated Statistical Methods and Data Analysis</p> <p>Revised Appendix A - Schedule of Events</p> <p>Revised Appendix B - Listing of Laboratory Assays</p> <p>Revised or Added Titration and Follow-up Flowcharts in Appendices C–F</p>

23 March 2012	Added Investigational Sites Removed Enrollment Limits Revised Eligibility Criteria (IC #3) Revised Eligibility Criteria (IC #7; Added EC #4) Added Exclusion Criteria (EC #5-7) Clarified Exclusion Criteria (Renumbered EC #10) Clarified Exclusion Criteria (Renumbered EC #17) Clarified Wording for Timing of Long-Term Maintenance Visits Added Run-in Period Other Antihypertensive Treatment Usage Clarified Exact Timing of RLY5016 Dosing When Dose is Adjusted (Treatment Initiation and Long-Term Maintenance Periods) Revised Blood Pressure Control Guidelines During the Treatment Initiation and Long-Term Maintenance Periods Revised Other Antihypertensive Treatment Usage During the Treatment Initiation Period Clarified Serum Potassium and Blood Pressure Monitoring and Control Procedures (Long-Term Maintenance Titration Algorithm) Inserted Rules for Withdrawal for Non-Responders (Long-Term Maintenance Titration Algorithm) Revised Concomitant Medication Usage During the Long-Term Maintenance Period Added Survival Follow-up Contact for Patients that Early Terminate (Telephone Calls) Revised Withdrawal Criteria Deleted Reference to "Study Manual" Clarified Exact Timing of Spironolactone and Losartan Initiation Revised Prohibited Concomitant Medication Text Revised Allowed Concomitant Medication Text Added New Criteria for Rescreening of Patients Added Serum Magnesium to New Confirmatory Local Lab Test at Screening (Cohort 3 only) Revised Appendix A - Schedule of Events Revised Appendix F – End of Treatment / Early Termination Flowchart
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported