



Clinical trial results:

A Two-Part, Single-Blind, Phase 3 Study Evaluating the Efficacy and Safety of Patiromer for the Treatment of Hyperkalemia

Summary

EudraCT number	2012-001956-20
Trial protocol	HU CZ SI BG IT DK
Global end of trial date	06 August 2013

Results information

Result version number	v1 (current)
This version publication date	04 April 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	RLY5016-301
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01810939
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	01 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2013
Global end of trial reached?	Yes
Global end of trial date	06 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A:

To evaluate the efficacy and safety of patiomer for the treatment of hyperkalemia (K+).

Part B:

To evaluate the effect of withdrawing patiomer on serum potassium control;

To assess whether chronic treatment with patiomer prevents the recurrence of hyperkalemia

To provide placebo-controlled safety data.

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	20 February 2013
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	Slovenia: 6
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Hungary: 33
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	Georgia: 79
Country: Number of subjects enrolled	Ukraine: 63
Country: Number of subjects enrolled	Serbia: 14
Country: Number of subjects enrolled	Croatia: 10
Worldwide total number of subjects	243
EEA total number of subjects	65

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)	112
From 65 to 84 years	131
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were 18 - 80 years of age with hyperkalemia, chronic kidney disease and on stable dose of at least one renin angiotensin aldosterone system inhibitor medication.

Period 1

Period 1 title	Part A Treatment Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Part A 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, 4.2 g or 8.4 g starting dose, orally, twice a day for 4 weeks

Number of subjects in period 1	Part A Patiromer
Started	243
Completed	219
Not completed	24
Consent withdrawn by subject	5
Adverse event, non-fatal	10
Protocol-specified withdrawal criteria (high K+)	3
Protocol-specified withdrawal criteria (eGFR)	2
Non-compliance with study drug	1
Protocol Violation	2
Protocol-specified withdrawal criteria (low K+)	1

Period 2

Period 2 title	Part B Placebo-Controlled Withdrawal
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
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Arm title	Part B Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo, orally, twice a day for 8 weeks

Arm title	Part B Patiromer
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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:

Subjects continued on the same daily patiromer dose as administered at the time of the Part A Week 4 Visit for 8 weeks

Number of subjects in period 2^[1]	Part B Placebo	Part B Patiromer
Started	52	55
Completed	30	45
Not completed	22	10
Adverse event, serious fatal	1	-
Physician decision	1	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	1
Protocol-specified withdrawal criteria (high K+)	14	2
Protocol-specified withdrawal criteria (K+ result)	2	1
Protocol-specified withdrawal criteria (eGFR)	1	1
Non-compliance with study drug	-	1

Lost to follow-up	-	1
Protocol-specified withdrawal criteria (low K+)	1	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: To be eligible for Part B, subjects had to meet all of the following: (1) baseline serum K+ at the beginning of Part A is ≥ 5.5 mEq/L, (2) completed the 4 weeks of dosing with Patiromer in Part A, (3) serum K+ at the Part A Week 4 visit in target range for Part A (≥ 3.8 mEq/L and < 5.1 mEq/L), (4) receiving Patiromer at a dose of 8.4 g/day to 50.4 g/day at the Part A Week 4 visit, and (5) still receiving treatment with a RAASi at the Part A Week 4 visit.

Baseline characteristics

Reporting groups

Reporting group title	Part A Treatment Period
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Reporting group description: -

Reporting group values	Part A Treatment Period	Total	
Number of subjects	243	243	
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)	112	112	
From 65-84 years	131	131	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	64.2		
full range (min-max)	29 to 80	-	
Gender categorical			
Units: Subjects			
Female	103	103	
Male	140	140	

End points

End points reporting groups

Reporting group title	Part A Patiromer
Reporting group description: -	
Reporting group title	Part B Placebo
Reporting group description: -	
Reporting group title	Part B Patiromer
Reporting group description: -	

Primary: Change in Serum Potassium from Part A Baseline to Part A Week 4

End point title	Change in Serum Potassium from Part A Baseline to Part A Week 4 ^[1]
End point description: Includes subjects in the intent to treat population of Part A who had either a local or central laboratory serum potassium result at baseline and at least one weekly post-baseline visit (i.e., Part A Week 1 or later) and excludes six subjects who had no result collected after Part A Day 3.	
End point type	Primary
End point timeframe: Part A Baseline to Part A Week 4	

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: Part A primary efficacy endpoint: The mean (SE) change in serum potassium from Part A Baseline to Part A Week 4 was -1.01 (0.031) mEq/L [95% CI: (-1.07, -0.95)]; this mean reduction in serum potassium was statistically significantly different from zero ($p < 0.001$).

End point values	Part A Patiromer			
Subject group type	Reporting group			
Number of subjects analysed	237 ^[2]			
Units: mEq/L				
least squares mean (standard error)	-1.01 (\pm 0.031)			

Notes:

[2] - Excludes six subjects who had no result collected after Part A Day 3.

Statistical analyses

No statistical analyses for this end point

Primary: Change in Serum Potassium from Part B Baseline

End point title	Change in Serum Potassium from Part B Baseline
End point description: Change in Serum Potassium from Part B Baseline to either: Part B Week 4 visit, if the subject's serum potassium remained ≥ 3.8 mEq/L and < 5.5 mEq/L up to the Part B Week 4 visit or the earliest Part B visit at which the subject's serum potassium was < 3.8 mEq/L or ≥ 5.5 mEq/L.	
End point type	Primary
End point timeframe: Part B Baseline to Part B Week 4 or first local laboratory serum potassium < 3.8 mEq/L or ≥ 5.5 mEq/L	

End point values	Part B Placebo	Part B Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	55		
Units: mEq/L				
median (inter-quartile range (Q1-Q3))	0.72 (0.22 to 1.22)	0 (-0.3 to 0.3)		

Statistical analyses

Statistical analysis title	Difference in Serum Potassium Change in Part B
Statistical analysis description:	
Test for difference between treatment groups in serum potassium change in Part B	
Comparison groups	Part B Placebo v Part B Patiromer
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Secondary: Proportion of Subjects with Serum Potassium ≥ 5.1 mEq/L in Part B

End point title	Proportion of Subjects with Serum Potassium ≥ 5.1 mEq/L in Part B
End point description:	
End point type	Secondary
End point timeframe:	
Part B Baseline to Part B Week 8	

End point values	Part B Placebo	Part B Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	55		
Units: percentage of participants	91	43		

Statistical analyses

Statistical analysis title	Difference between Groups in Proportion ≥ 5.1 mEq/L
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Statistical analysis description:

Test for difference between treatment groups in proportion with serum potassium ≥ 5.1 mEq/L

Comparison groups	Part B Placebo v Part B Patiromer
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mantel-Haenszel

Secondary: Proportion of Subjects with Serum Potassium ≥ 5.5 mEq/L in Part B

End point title	Proportion of Subjects with Serum Potassium ≥ 5.5 mEq/L in Part B
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End point description:

End point type	Secondary
End point timeframe:	Part B Baseline to Part B Week 8

End point values	Part B Placebo	Part B Patiromer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	55		
Units: percentage of participants	60	15		

Statistical analyses

Statistical analysis title	Difference between Groups in Proportion ≥ 5.5 mEq/L
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Statistical analysis description:

Test for difference between treatment groups in proportion with serum potassium ≥ 5.5 mEq/L

Comparison groups	Part B Placebo v Part B Patiromer
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mantel-Haenszel

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 2 weeks after end of treatment

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	Part A Patiromer
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Reporting group description:

Participants were administered 4.2 g or 8.4 g starting dose of patiromer, orally, twice daily, with dose adjustment based on serum potassium, for 4 weeks

Reporting group title	Part B Patiromer
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Reporting group description:

Participants continued on the same daily Part A patiromer dose as administered at the time of the Part A Week 4 Visit for 8 weeks

Reporting group title	Part B Placebo
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Reporting group description:

Participants were administered placebo, orally, twice a day for 8 weeks

Serious adverse events	Part A Patiromer	Part B Patiromer	Part B Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 243 (1.23%)	0 / 55 (0.00%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Anticoagulation drug level below therapeutic			
subjects affected / exposed	1 / 243 (0.41%)	0 / 55 (0.00%)	0 / 52 (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 disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 243 (0.41%)	0 / 55 (0.00%)	0 / 52 (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 disorders			
Thrombosis mesenteric vessel			

subjects affected / exposed	0 / 243 (0.00%)	0 / 55 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders			
Renal failure chronic			
subjects affected / exposed	1 / 243 (0.41%)	0 / 55 (0.00%)	0 / 52 (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
Infections and infestations			
Escherichia bacteraemia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 55 (0.00%)	0 / 52 (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
Urinary tract infection			
subjects affected / exposed	1 / 243 (0.41%)	0 / 55 (0.00%)	0 / 52 (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
Endocarditis enterococcal			
subjects affected / exposed	1 / 243 (0.41%)	0 / 55 (0.00%)	0 / 52 (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

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

Non-serious adverse events	Part A Patiromer	Part B Patiromer	Part B Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 243 (13.58%)	5 / 55 (9.09%)	8 / 52 (15.38%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 243 (1.65%)	0 / 55 (0.00%)	3 / 52 (5.77%)
occurrences (all)	4	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 243 (0.82%)	2 / 55 (3.64%)	4 / 52 (7.69%)
occurrences (all)	2	2	4

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	26 / 243 (10.70%)	2 / 55 (3.64%)	0 / 52 (0.00%)
occurrences (all)	26	2	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 243 (0.41%)	1 / 55 (1.82%)	3 / 52 (5.77%)
occurrences (all)	1	1	3

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