



Clinical trial results:

A Phase 2b, double-blind, randomized, placebo-controlled study of RVT-101 in subjects with dementia with Lewy bodies (DLB).

Summary

EudraCT number	2015-005495-19
Trial protocol	ES NL IT
Global end of trial date	04 December 2017

Results information

Result version number	v1 (current)
This version publication date	16 January 2019
First version publication date	16 January 2019

Trial information

Trial identification

Sponsor protocol code	RVT-101-2001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02669433
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Axovant Sciences Ltd.
Sponsor organisation address	2 Church Street, Hamilton, Bermuda,
Public contact	Clinical Trial Information Dept., Axovant Sciences, Inc, +34 900834223, Registroespanoldeestudiosclnicos@druginfo.com
Scientific contact	Clinical Trial Information Dept., Axovant Sciences, Inc, +34 900834223, Registroespanoldeestudiosclnicos@druginfo.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	19 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2017
Global end of trial reached?	Yes
Global end of trial date	04 December 2017
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 assess the effects of 35-mg and 70-mg doses of RVT-101 compared with placebo on the primary endpoint of motor function as measured by the Unified Parkinson's Disease Rating Scale – Part III (UPDRS-III). The UPDRS-III is a gold standard measurement for capturing pharmacologic effects on parkinsonian motor symptoms. The secondary objectives are to assess the effects of RVT-101 compared to placebo on cognition as measured by the ADAS-Cog 11 and global function as measured by the CIBIC+.

Protection of trial subjects:

Subjects were required to provide full written informed consent prior to the performance of any protocol specified procedure; or if unable to provide informed consent due to cognitive status, subject has provided assent and a legally acceptable representative has provided full written informed consent on behalf of the subject. Collection of AEs and SAEs were collected at the time of informed consent and continued until the follow-up contact. SAEs that were spontaneously reported by the subject or subject representative or discovered by the investigator or designee after the follow-up visit and up to 30 days after the last dose of investigational product were collected and reported. Subjects were withdrawn from the study based on consultation between the principal investigator and Medical Monitor, with the ultimate decision by the principal investigator or subject. Study safety data was periodically reviewed by an independent data monitoring committee.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	United Kingdom: 29
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	Italy: 28
Country: Number of subjects enrolled	United States: 144
Country: Number of subjects enrolled	Canada: 6
Worldwide total number of subjects	269
EEA total number of subjects	119

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)	34
From 65 to 84 years	229
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened for eligibility during the Screening Period. An ICF was signed by each subject or by the caregiver with subject assent. Consent forms were also signed by the caregiver before any study specific procedures were performed. Subjects were screened according to study inclusion/exclusion criteria.

Period 1

Period 1 title	Double-Blind (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This study included a 24-week Double-Blind Treatment Period when neither subjects nor investigators knew which of the three treatments the subject was receiving. Subjects were informed that they would receive placebo at some point during the study but they did not know when this would be. Subjects were not informed of the transition from the Single-Blind Run-In Period to the Double-Blind Treatment Period. RVT 101 and placebo were provided as tablets that are indistinguishable.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects dosed with two Placebo tablets

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

Dosage and administration details:

Placebo was administered as pink film-coated round tablets. Subjects were instructed to take 2 tablets orally daily at bedtime without regard to food for 24 weeks.

Arm title	RVT-101 35 mg
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Arm description:

Subjects dosed with one Placebo tablet + 1 35 mg tablet of RVT-101

Arm type	Experimental
Investigational medicinal product name	RVT-101
Investigational medicinal product code	
Other name	Intepirdine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RVT-101 was administered as pink film-coated round 35-mg tablets. Subjects were instructed to take tablets orally each morning without regard to food for 24 weeks.

Arm title	RVT-101 70 mg
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Arm description:

Subjects dosed with two RVT-101 35 mg tablets

Arm type	Experimental
Investigational medicinal product name	RVT-101
Investigational medicinal product code	
Other name	Intepirdine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RVT-101 was administered as pink film-coated round 35-mg tablets. Subjects were instructed to take tablets orally each morning without regard to food for 24 weeks.

Number of subjects in period 1	Placebo	RVT-101 35 mg	RVT-101 70 mg
Started	91	89	89
Safety Population	91	89	88
Intent-To-Treat Population	89	89	87
Per-Protocol Population	78	79	82
Completed	76	75	74
Not completed	15	14	15
Adverse event, serious fatal	1	1	2
Consent withdrawn by subject	5	1	-
Physician decision	1	1	-
Adverse event, non-fatal	5	6	8
Death	-	1	1
Sponsor Termination	1	-	1
Caregiver Withdrew Consent	1	-	2
Disease Progression	1	-	-
Protocol deviation	-	4	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects dosed with two Placebo tablets	
Reporting group title	RVT-101 35 mg
Reporting group description:	
Subjects dosed with one Placebo tablet + 1 35 mg tablet of RVT-101	
Reporting group title	RVT-101 70 mg
Reporting group description:	
Subjects dosed with two RVT-101 35 mg tablets	

Reporting group values	Placebo	RVT-101 35 mg	RVT-101 70 mg
Number of subjects	91	89	89
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	9	13
From 65-84 years	76	79	74
85 years and over	3	1	2
Age continuous			
Units: years			
arithmetic mean	73.6	73.0	73.0
full range (min-max)	59 to 86	55 to 85	55 to 86
Gender categorical			
Units: Subjects			
Female	20	22	15
Male	71	67	74

Reporting group values	Total		
Number of subjects	269		
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)	34		

From 65-84 years	229		
85 years and over	6		

Age continuous			
Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	57		
Male	212		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects dosed with two Placebo tablets	
Reporting group title	RVT-101 35 mg
Reporting group description:	
Subjects dosed with one Placebo tablet + 1 35 mg tablet of RVT-101	
Reporting group title	RVT-101 70 mg
Reporting group description:	
Subjects dosed with two RVT-101 35 mg tablets	

Primary: Unified Parkinson's Disease Rating Scale – Part III (UPDRS Part III) Score Change from Baseline to Week 24

End point title	Unified Parkinson's Disease Rating Scale – Part III (UPDRS Part III) Score Change from Baseline to Week 24
End point description:	
The primary endpoint was to assess the effects of intepirdine versus placebo on the UPDRS Part III after 24 weeks of treatment. UPDRS Part III scores range from 0 to 108, with higher scores indicating worse outcome.	
End point type	Primary
End point timeframe:	
Baseline, 24 weeks	

End point values	Placebo	RVT-101 35 mg	RVT-101 70 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	72	69	
Units: NA	72	72	69	

Statistical analyses

Statistical analysis title	Repeated Measures Analysis
Statistical analysis description:	
Placebo - active	
Comparison groups	Placebo v RVT-101 35 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.158 ^[1]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	0.79

Notes:

[1] - The threshold for statistical significance was $p=0.05$

Statistical analysis title	Repeated Measures Analysis
Statistical analysis description:	
Placebo - active	
Comparison groups	RVT-101 70 mg v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6069 [2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.08
upper limit	3.55

Notes:

[2] - The threshold for statistical significance was $p=0.05$

Secondary: Alzheimer's Disease Assessment Scale – Cognitive Subscale 11 Items (ADAS-Cog-11) Score Change From Baseline to Week 24

End point title	Alzheimer's Disease Assessment Scale – Cognitive Subscale 11 Items (ADAS-Cog-11) Score Change From Baseline to Week 24
End point description:	
The 11-item ADAS-Cog assesses a range of cognitive abilities including memory, comprehension, orientation in time and place, and spontaneous speech. The ADAS-Cog-11 total score range is from 0 to 70, with a higher score indicating more severe cognitive impairment.	
End point type	Secondary
End point timeframe:	
Baseline, 24 weeks	

End point values	Placebo	RVT-101 35 mg	RVT-101 70 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	73	71	
Units: NA	73	73	71	

Statistical analyses

Statistical analysis title	Repeated Measures Analysis
Statistical analysis description:	
Placebo - active	
Comparison groups	Placebo v RVT-101 35 mg
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6531 ^[3]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.55
upper limit	1.6

Notes:

[3] - The threshold for statistical significance was $p=0.05$

Statistical analysis title	Repeated Measures Analysis
Statistical analysis description:	
Placebo - active	
Comparison groups	Placebo v RVT-101 70 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5274 ^[4]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	2.75

Notes:

[4] - The threshold for statistical significance was $p=0.05$

Primary:

Secondary: Clinical Global Impression of Change - Plus Caregiver Interview (CIBIC+) Score at Week 24

End point title	Clinical Global Impression of Change - Plus Caregiver Interview (CIBIC+) Score at Week 24
End point description:	
To assess the effects of RVT-101 versus placebo on global function as measured by the CIBIC+ after 24 weeks of treatment	
End point type	Secondary
End point timeframe:	
Baseline, 24 weeks	

End point values	Placebo	RVT-101 35 mg	RVT-101 70 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	75	74	72	
Units: NA	75	74	72	

Statistical analyses

Statistical analysis title	Repeated Measures Analysis
Statistical analysis description: Placebo - active	
Comparison groups	Placebo v RVT-101 35 mg
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3953 ^[5]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.5

Notes:

[5] - The threshold for statistical significance was p=0.05

Statistical analysis title	Repeated Measures Analysis
Statistical analysis description: Placebo - active	
Comparison groups	Placebo v RVT-101 70 mg
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7008
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.42

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Collection of AEs and SAEs will begin at the time a subject signs informed consent and continues until the follow-up contact.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	RVT-101 35 mg
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Reporting group description: -

Reporting group title	RVT 70 mg
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Reporting group description: -

Serious adverse events	Placebo	RVT-101 35 mg	RVT 70 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 91 (12.09%)	11 / 89 (12.36%)	13 / 88 (14.77%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	2 / 91 (2.20%)	0 / 89 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Prostatic adenoma			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Injury, poisoning and procedural complications			

Concussion			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Facial bones fracture			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Spinal compression fracture			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Subdural haematoma			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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 flutter			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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

Trifascicular block			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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			
Rectal haemorrhage			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Enteritis			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Volvulus			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	2 / 91 (2.20%)	0 / 89 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Hallucination, visual			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Neuropsychiatric syndrome			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 91 (2.20%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	2 / 88 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 91 (1.10%)	1 / 89 (1.12%)	0 / 88 (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
Escherichia urinary tract infection			

subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Pyelonephritis			
subjects affected / exposed	0 / 91 (0.00%)	0 / 89 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 89 (1.12%)	0 / 88 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (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
Hyponatraemia			
subjects affected / exposed	1 / 91 (1.10%)	0 / 89 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	1 / 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	Placebo	RVT-101 35 mg	RVT 70 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 91 (72.53%)	69 / 89 (77.53%)	59 / 88 (67.05%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	19 / 91 (20.88%)	17 / 89 (19.10%)	18 / 88 (20.45%)
occurrences (all)	19	17	18

Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 91 (5.49%)	1 / 89 (1.12%)	2 / 88 (2.27%)
occurrences (all)	5	1	2
Orthostatic hypotension			
subjects affected / exposed	12 / 91 (13.19%)	3 / 89 (3.37%)	5 / 88 (5.68%)
occurrences (all)	12	3	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 91 (4.40%)	3 / 89 (3.37%)	5 / 88 (5.68%)
occurrences (all)	4	3	5
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 91 (5.49%)	9 / 89 (10.11%)	6 / 88 (6.82%)
occurrences (all)	5	9	6
Diarrhoea			
subjects affected / exposed	3 / 91 (3.30%)	7 / 89 (7.87%)	5 / 88 (5.68%)
occurrences (all)	3	7	5
Nausea			
subjects affected / exposed	2 / 91 (2.20%)	4 / 89 (4.49%)	5 / 88 (5.68%)
occurrences (all)	2	4	5
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	7 / 91 (7.69%)	8 / 89 (8.99%)	1 / 88 (1.14%)
occurrences (all)	7	8	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 91 (3.30%)	5 / 89 (5.62%)	2 / 88 (2.27%)
occurrences (all)	3	5	2
Confusional state			
subjects affected / exposed	3 / 91 (3.30%)	5 / 89 (5.62%)	5 / 88 (5.68%)
occurrences (all)	3	5	5
Hallucination, visual			
subjects affected / exposed	4 / 91 (4.40%)	6 / 89 (6.74%)	3 / 88 (3.41%)
occurrences (all)	4	6	3
Musculoskeletal and connective tissue disorders			

Back pain subjects affected / exposed occurrences (all)	0 / 91 (0.00%) 0	7 / 89 (7.87%) 7	5 / 88 (5.68%) 5
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 91 (4.40%) 4	7 / 89 (7.87%) 7	7 / 88 (7.95%) 7
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 91 (6.59%) 6	3 / 89 (3.37%) 3	2 / 88 (2.27%) 2

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