Clinical trial results:
A Long-Term, Open-Label Extension Study of the Safety and Tolerability of RVT-101 in Subjects with Alzheimer's Disease

Summary

EudraCT number	2016-000587-42
Trial protocol	CZ SK ES BG DE GB HR IT
Global end of trial date	12 March 2018

Results information

Result version number	v1 (current)
This version publication date	28 March 2019
First version publication date	28 March 2019

Trial information

Trial identification

Sponsor protocol code	RVT-101-3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02586909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Axovant Sciences
Sponsor organisation address	Viaduktstrasse 8, Basel, Switzerland, 4051
Public contact	Project Management, Worldwide Clinical Trials , +44 207121 6161,
Scientific contact	Project Management, Worldwide Clinical Trials , +44 207121 6161,

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	12 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2018
Global end of trial reached?	Yes
Global end of trial date	12 March 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and tolerability of RVT-101

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 Subjects were withdrawn from the study based on consultation between the principal investigator and Medical Monitor, with the ultimate decision by the principal investigator or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	26 April 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	Argentina: 103
Country: Number of subjects enrolled	Australia: 31
Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	Chile: 48
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Singapore: 16
Country: Number of subjects enrolled	Serbia: 21
Country: Number of subjects enrolled	Taiwan: 16
Country: Number of subjects enrolled	United States: 281
Country: Number of subjects enrolled	Poland: 47
Country: Number of subjects enrolled	Slovakia: 42
Country: Number of subjects enrolled	Spain: 65
Country: Number of subjects enrolled	United Kingdom: 164
Country: Number of subjects enrolled	Croatia: 30
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Czech Republic: 53

Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 55
Country: Number of subjects enrolled	Italy: 61
Worldwide total number of subjects	1099
EEA total number of subjects	537

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)	158
From 65 to 84 years	907
85 years and over	34

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This is a multi-center, open-label, extension study in subjects with AD who have completed the 24-week, double-blind, placebo-controlled, lead-in study (RVT-101-3001). Subjects who have completed the double-blind lead-in study will be enrolled in this study.

Period 1

Period 1 title	Open Label Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to Intepirdine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	RVT-101 35 mg
Investigational medicinal product code	
Other name	Intepirdine 35 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Take 1 tablet orally each morning without regard to food

Arm title	Intepirdine to Intepirdine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	RVT-101 35 mg
Investigational medicinal product code	
Other name	Intepirdine 35 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Take 1 tablet orally each morning without regard to food

Number of subjects in period 1	Placebo to Intepirdine	Intepirdine to Intepirdine
Started	538	561
Completed	80	71
Not completed	458	490
Adverse event, serious fatal	3	4
Consent withdrawn by subject	36	39
Physician decision	14	11

Adverse event, non-fatal	22	22
Sponsor Termination	338	369
Sponsor Decision	2	3
Lost to follow-up	3	3
Advice From Hrec	7	5
Caregiver Withdrew Consent	13	8
Ae On V8/V1 Recorded Under 3001 Protocol	-	1
Lack of efficacy	19	20
Protocol deviation	1	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo to Intepirdine
Reporting group description: -	
Reporting group title	Intepirdine to Intepirdine
Reporting group description: -	

Reporting group values	Placebo to Intepirdine	Intepirdine to Intepirdine	Total
Number of subjects	538	561	1099
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	73.0	73.2	
standard deviation	± 7.51	± 7.60	-
Gender categorical Units: Subjects			
Female	336	340	676
Male	202	221	423
Ethnicity Units: Subjects			
Hispanic or Latino	84	109	193
Not Hispanic or Latino	448	449	897
Missing	6	3	9

End points

End points reporting groups

Reporting group title	Placebo to Intepirdine
Reporting group description: -	
Reporting group title	Intepirdine to Intepirdine
Reporting group description: -	

Primary: At Least one On-Treatment Adverse Event (OTAE)

End point title	At Least one On-Treatment Adverse Event (OTAE)[1]
End point description:	
End point type	Primary
End point timeframe:	
52 weeks	

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: The objective of this study was to assess the long-term safety and tolerability of RVT-101 (intepirdine) in subjects with AD, and the study was terminated early on 11 January 2018 because intepirdine did not meet its primary endpoint for Study RVT-101-3001 (the lead-in study). Thus, no formal statistical analyses were performed for the primary endpoint.

End point values	Placebo to Intepirdine	Intepirdine to Intepirdine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	538	561		
Units: Subjects	263	286		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 52 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Placebo to Intepirdine
Reporting group description: -	
Reporting group title	Intepirdine to Intepirdine
Reporting group description: -	

Serious adverse events	Placebo to Intepirdine	Intepirdine to Intepirdine	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 538 (7.06%)	49 / 561 (8.73%)	
number of deaths (all causes)	4	6	
number of deaths resulting from adverse events	4	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	2 / 538 (0.37%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			

subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer female			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage I			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycosis fungoides			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			

subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

Hypothermia			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervix disorder			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 538 (0.00%)	2 / 561 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	2 / 538 (0.37%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	3 / 10	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusion			

subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	1 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Full blood count decreased			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 538 (0.56%)	2 / 561 (0.36%)	
occurrences causally related to treatment / all	1 / 26	1 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Humerus fracture			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 538 (0.00%)	3 / 561 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Atrial fibrillation			

subjects affected / exposed	2 / 538 (0.37%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve stenosis			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic stroke			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral haemorrhage			

subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia of the Alzheimer's type, with delirium			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 538 (0.37%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	1 / 5	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 538 (0.37%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	2 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	3 / 10	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	3 / 538 (0.56%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 538 (0.19%)	3 / 561 (0.53%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastroenteritis			
subjects affected / exposed	1 / 538 (0.19%)	2 / 561 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 538 (0.00%)	2 / 561 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 538 (0.19%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	1 / 24	3 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 538 (0.00%)	2 / 561 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchitis			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 538 (0.00%)	1 / 561 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 538 (0.19%)	0 / 561 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 538 (0.37%)	3 / 561 (0.53%)	
occurrences causally related to treatment / all	1 / 4	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo to Intepirdine	Intepirdine to Intepirdine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 538 (15.99%)	88 / 561 (15.69%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	23 / 538 (4.28%)	26 / 561 (4.63%)	
occurrences (all)	26	28	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 538 (1.86%)	7 / 561 (1.25%)	
occurrences (all)	12	7	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 538 (1.49%)	14 / 561 (2.50%)	
occurrences (all)	8	14	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	23 / 538 (4.28%)	22 / 561 (3.92%)	
occurrences (all)	24	23	
Nasopharyngitis			
subjects affected / exposed	11 / 538 (2.04%)	12 / 561 (2.14%)	
occurrences (all)	11	12	
Upper respiratory tract infection			
subjects affected / exposed	11 / 538 (2.04%)	7 / 561 (1.25%)	
occurrences (all)	11	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2016	Protocol RVT-101-3002 version 2.0 includes the following changes to protocol version 1.0 dated 18 February 2016: the Dependence Scale (DS) and EuroQOL 5 dimensions questionnaire (EQ-5D) have been added as efficacy assessments at Visits 1, 5, and 7; caregiver requirements have been added; and administrative changes were made for clarification.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 January 2018	This study was terminated early on 9 January 2018 because RVT-101 (intepirdine) did not meet its primary endpoint for Study RVT-101-3001 (the lead-in study).	-

Notes:

Limitations and caveats

None reported