



Clinical trial results:

A Long-Term Extension Study of the Safety and Tolerability of RVT-101 in Subjects with Dementia with Lewy Bodies (DLB)

Summary

EudraCT number	2016-002412-40
Trial protocol	GB ES NL IT
Global end of trial date	09 February 2018

Results information

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

Trial information

Trial identification

Sponsor protocol code	RVT-101-2002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02928445
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Axovant Sciences
Sponsor organisation address	Viaduktstrasse 8, Basel, Switzerland, 4051
Public contact	Clinical Trial Information Dept., Axovant Sciences, +41 43 215 59 99,
Scientific contact	Clinical Trial Information Dept., Axovant Sciences, +41 43 215 59 99,

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	09 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2018
Global end of trial reached?	Yes
Global end of trial date	09 February 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 35 mg and 70 mg RVT-101 in subjects with DLB

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 Subjects were withdrawn from the study based on consultation between the principal investigator and Medical Monitor, with the ultimate decision by the principal investigator or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	03 October 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: 4
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	United States: 114
Worldwide total number of subjects	213
EEA total number of subjects	95

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	29
From 65 to 84 years	181
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who were randomized to the treatment arms RVT-101 35 mg and RVT-101 70 mg in the lead-in study (RVT-101-2001) will remain in those same treatment groups for this study, while subjects who were randomized to placebo in Study RVT-101-2001 will be assigned to the RVT-101 70 mg treatment group.

Period 1

Period 1 title	Double-Blind Treatment (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:

Treatment assignments for this study were double-blind, meaning neither subjects nor investigators knew which of the two treatments the subject was receiving. If this study was ongoing when the database for the lead-in study (RVT-101-2001) was locked and unblinded, this study became double-blind, Sponsor-open, meaning the subject and investigator did not know what treatment assignment he/she had been given but the Sponsor and its representatives did.

Arms

Are arms mutually exclusive?	Yes
Arm title	RVT-101 35 mg

Arm description:

RVT-101 35 mg once daily

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:

RVT-101 35 mg once daily

Arm title	RVT-101 70 mg
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Arm description:

RVT-101 70 mg once daily

Arm type	Experimental
Investigational medicinal product name	RVT-101 70 mg
Investigational medicinal product code	
Other name	Intepirdine 70 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RVT-101 70 mg once daily

Number of subjects in period 1	RVT-101 35 mg	RVT-101 70 mg
Started	71	142
Completed	16	26
Not completed	55	116
Adverse event, serious fatal	-	2
Consent withdrawn by subject	1	5
Physician decision	1	-
Adverse event, non-fatal	3	11
Lost to follow-up	-	6
Sponsor termination	49	87
Caregiver Withdrew Consent	-	4
Protocol deviation	1	1

Baseline characteristics

Reporting groups

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

RVT-101 35 mg once daily

Reporting group title	RVT-101 70 mg
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Reporting group description:

RVT-101 70 mg once daily

Reporting group values	RVT-101 35 mg	RVT-101 70 mg	Total
Number of subjects	71	142	213
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	72.4	72.6	
standard deviation	± 5.98	± 6.58	-
Gender categorical Units: Subjects			
Female	18	28	46
Male	53	114	167
Ethnicity Units: Subjects			
Hispanic or Latino	5	3	8
Not Hispanic or Latino	66	137	203
Unknown or Not Reported	0	2	2

End points

End points reporting groups

Reporting group title	RVT-101 35 mg
Reporting group description: RVT-101 35 mg once daily	
Reporting group title	RVT-101 70 mg
Reporting group description: RVT-101 70 mg once daily	

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: 24 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 DLB, and the study was terminated early on 9 January 2018 because intepirdine did not meet its primary endpoint for Study RVT-101-2001 (the lead-in study). Thus, no formal statistical analyses were performed for the primary endpoint.

End point values	RVT-101 35 mg	RVT-101 70 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	142		
Units: Participants				
At Least one On-Treatment Adverse Event (OTAE)	54	103		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 weeks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

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

Reporting group title	RVT-101 70 mg
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Reporting group description: -

Serious adverse events	RVT-101 35 mg	RVT-101 70 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 71 (12.68%)	17 / 142 (11.97%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of bladder			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Gait disturbance			

subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			

subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 3	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric decompensation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	2 / 14	3 / 36	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Dementia with Lewy bodies			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Encephalopathy			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radial nerve palsy			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	2 / 142 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	1 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 71 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 71 (2.82%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RVT-101 35 mg	RVT-101 70 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 71 (63.38%)	86 / 142 (60.56%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	14 / 71 (19.72%)	35 / 142 (24.65%)	
occurrences (all)	14	36	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 71 (5.63%)	10 / 142 (7.04%)	
occurrences (all)	4	10	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	4 / 71 (5.63%)	4 / 142 (2.82%)	
occurrences (all)	4	4	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 71 (1.41%)	8 / 142 (5.63%)	
occurrences (all)	1	8	
Diarrhoea			
subjects affected / exposed	3 / 71 (4.23%)	10 / 142 (7.04%)	
occurrences (all)	3	10	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	6 / 71 (8.45%)	3 / 142 (2.11%)	
occurrences (all)	6	3	
Insomnia			
subjects affected / exposed	4 / 71 (5.63%)	3 / 142 (2.11%)	
occurrences (all)	4	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 71 (5.63%)	3 / 142 (2.11%)	
occurrences (all)	4	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 71 (9.86%)	1 / 142 (0.70%)	
occurrences (all)	7	1	

Urinary tract infection subjects affected / exposed occurrences (all)	6 / 71 (8.45%) 6	7 / 142 (4.93%) 7	
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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? Yes

Date	Interruption	Restart date
09 January 2018	This study was terminated early on 9 January 2018 because RVT-101 (intepirdine) did not meet its primary endpoint for Study RVT-101-2001 (the lead-in study).	-

Notes:

Limitations and caveats

None reported