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

Published: 25-04-2016
Last updated: 31-12-2024

Primary• To assess the effects of RVT-101 versus placebo on global function as measured by the Clinician*s Interview-Based Impression of Change Plus Caregiver Input (CIBIC+) after 24 weeks of treatment• To assess the effects of RVT-101 versus...

Ethical review	Approved WMO
Status	Completed
Health condition type	Mental impairment disorders
Study type	Observational invasive

Summary

ID

NL-OMON43126

Source
ToetsingOnline

Brief title
RVT-101-2001

Condition

- Mental impairment disorders

Synonym
Dementia with Lewy Bodies. Dementia with Lewy bodies (DLB) is a type of dementia that shares symptoms with both Alzheimer's disease and Parkinson's disease.

Research involving
Human

Sponsors and support

Primary sponsor: Axovant Sciences, Inc
Source(s) of monetary or material Support: Axovant

Intervention

Keyword: dementia with Lewy bodies (DLB)

Outcome measures

Primary outcome

Primary efficacy endpoint: The primary efficacy endpoints will be an assessment of cognition and global function at Week 24. Change from Baseline to Week 24 in cognition will be measured by a composite z-score of 7 domains of the CDR computerized assessment system (Power of Attention, Continuity of Attention, Quality of Working Memory, Quality of Episodic Memory, Speed of Memory, Cognitive Reaction Time and Reaction Time Variability). Global function at Week 24 will be measured by the CIBIC+.

Secondary outcome

Secondary efficacy endpoints: Instrumental activities of daily living will be measured by the instrumental subscale of the ADCS-ADL as a key secondary endpoint. Additional secondary endpoints are as described above in Objectives.

Study description

Background summary

The purpose of this study is to investigate how well RVT-101 works to improve cognitive and overall function as well as to investigate the safety of RVT-101. It is believed that patients with dementia with Lewy bodies have an imbalance of acetylcholine, which is a chemical in the brain thought to be responsible for cognition. RVT-101 promotes the release of this chemical. Therefore,

RVT-101 is being tested in this Phase 2b study to evaluate whether it can help cognition and overall function in patients with dementia with Lewy bodies.

Study objective

Primary
• To assess the effects of RVT-101 versus placebo on global function as measured by the Clinician*s Interview-Based Impression of Change Plus Caregiver Input (CIBIC+) after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on cognition as measured by the composite z-score of the 7 domains of the Cognitive Drug Research (CDR) computerized assessment system after 24 weeks of treatment (CDR domains include Power of Attention, Continuity of Attention, Quality of Working Memory, Quality of Episodic Memory, Speed of Memory, Cognitive Reaction Time and Reaction Time Variability)

Secondary
• To assess the effects of RVT-101 versus placebo on attention, as measured by the z-score of the Power of Attention (PoA) domain of the CDR System after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on instrumental activities of daily living as measured by the instrumental subscale of the Alzheimer*s Disease Cooperative Study - Activities of Daily Living (ADCS-ADL) scale after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on cognition, including amnestic aspects of cognition, as measured by the ADAS-cog-13 scale after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on executive function as assessed by the Controlled Oral Word Association Test (COWAT) after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on cognitive function as measured by a composite z-score combining the 7 domains for the CDR System and the COWAT after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on hallucinations and delusions as measured by a 2-item subscore on the Neuropsychiatric Inventory (NPI), which is the sum of the scores for the hallucinations and delusions domains (Parts A and B), after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on visual hallucinations as measured by the total severity score and distress score of the North-East Visual Hallucinations Interview (NEVHI) after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on fluctuations in cognition using the Clinician Assessment of Fluctuation (CAF)
after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on an analysis of responders based on pre-specified efficacy evaluations
• To assess the effects of RVT-101 versus placebo on subject dependence with the dependence scale (DS) after 24 weeks of treatment

• To assess the safety and tolerability of RVT-101
• To estimate the pharmacokinetic (PK) parameters of RVT-101 and explore relationships to efficacy or safety endpoints, as appropriate

Exploratory
• To assess the effects of RVT-101 versus placebo on quality of life as measured by the EuroQual-5D-5L (EQ-5D-5L) after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on sleep-related behaviors as measured by the modified Circadian Sleep Inventory (CSI)
• To assess the effects of RVT-101 versus placebo on each domain and subtest of the CDR computerized assessment system after 24 weeks of treatment
• To assess the effects of RVT-101 versus placebo on depression and anxiety as measured by a 2-item subscore on the NPI, which is the sum of the scores for the depression/dysphoria and anxiety domains (Parts D & E) after 24 weeks of treatment

Study design

This is a multi-center, double-blind, randomized, placebo-controlled, parallel-group study in patients with probable DLB. The efficacy and safety of RVT-101 at doses of 70 mg and 35 mg daily will be evaluated over a 24-week treatment period in subjects with probable DLB with or without existing background DLB therapy. All subjects who are on stable doses of other background therapies for dementia and/or hallucinations associated with DLB will continue those regimens unchanged for the duration of the study. Subjects who are not on background DLB therapies at the time of screening will also be eligible for participation. All subjects will refrain from starting additional DLB treatments during the course of the study. The randomization ratio will be 1:1:1 (70 mg RVT-101: 35 mg RVT-101: placebo).
Randomization will be stratified according to Baseline MMSE score in the groupings of 14-17 points, 18-21 points and 22-26 points and according to whether subjects are or are not taking a cholinesterase inhibitor as a concomitant medication.
During double-blind treatment, there will be weekly clinical assessments for the first two weeks of treatment, bi-weekly assessments until Week 12 and every six weeks thereafter. For certain visits, subjects may have the option of whether to have assessments performed at the clinical study site or by a trained, visiting nurse in their own home.
An independent Safety Monitoring Committee (SMC) will review interim safety data accumulated after approximately 30 subjects have completed 4 weeks of double-blind treatment and throughout the study at points specified in the SMC Charter. The SMC will provide their recommendation regarding the acceptability of reducing the visit frequency by skipping certain visits for both newly enrolled subjects and subjects active in the study at the time of the SMC recommendation. Study enrollment will not be stopped or slowed to wait for the SMC recommendation and will proceed as planned with all visits until the SMC

recommendation is made.

Study burden and risks

Burden, - questionnaires blood drawn at every visit, physical exam. See section 8.3 Study assessments and procedures van protocol v2.0 dd 19Feb2016.

As with taking any drug, there is a risk of allergic reaction. Some things that may happen during an allergic reaction are:
• Rash or hives
• Having a hard time breathing
• Wheezing when you breathe
• Sudden change in blood pressure, which may make you feel dizzy or lightheaded
• Swelling around the mouth, throat or eyes
• Fast pulse
• Sweating

The study may provide scientific data useful in the future.
RVT-101 is in this phase 2b study tested to assess whether the drug can promote cognitive and overall functioning in patients with Lewy Body Dementia.

Contacts

Public
Axovant Sciences, Inc

West, 4th Floor, 37th Street 320
New York 10018
US
Scientific
Axovant Sciences, Inc

West, 4th Floor, 37th Street 320
New York 10018
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) Male or female subject with a clinical diagnosis of DLB established for a minimum of 2 months prior to Visit 1 and who currently meet consensus criteria as determined by the PI by having dementia and either a) or b) below:
a) At least two of the following three Core Criteria: i) Fluctuating cognition,
ii) Recurrent visual hallucinations, or iii) Spontaneous features of parkinsonism.
b) One of the Core Criteria above and as least one of the following three Suggestive Criteria:
i) REM Sleep Behavior Disorder,
ii) Severe Neuroleptic Sensitivity, or iii) Low dopamine transporter uptake in basal ganglia on single photon emission computed tomography (SPECT) or positron emission tomography (PET) scan as determined by the investigator (SPECT or PET must have been performed in the 12 months prior to the Screening Visit otherwise it must be repeated prior to the Run-In Period).
2) Subject has an MMSE score of 14 to 26, inclusive, at Screening.
In addition, the MMSE score at Baseline (Visit 3) must not have declined by 4 points or more from the Visit 2 MMSE score. For subjects with an MMSE score at Baseline (Visit 3) of 4 or more points lower than their Visit 2 MMSE score, the Run-In period may be extended for 1 to 10 days . If, after the first extension to the Run-In Period, the subject still does not meet the MMSE stability criterion, the Run-In period may again be extended for an additional 1 to 10 days. No more than 2 extensions to the Run-In Period will be allowed. If this MMSE stability requirement is not met after 2 extensions of the Run-In Period, the subject will be discontinued from the study (see also Section 8.1).
3) If the subject is currently receiving any of the following medications, the treatment regimen has been stable (i.e., no changes in the type of drug, dose or frequency of dosing) for at least 30 days prior to the Screening Visit and there is no intent to change this treatment regimen for the duration of the study. Acetylcholinesterase inhibitors (i.e., donepezil, galantamine, rivastigmine, tacrine) Memantine Axona® (caprylidene) Antidepressants (other than MAO inhibitors) Thyroid hormones
Atypical antipsychotics (e.g., quetiapine) .Benzodiazepines and other sedatives/hypnotics
4) Subject is 50 to 85 years of age, inclusive, at the time of the Screening Visit.
5) Female subjects must be:
a) Of non-childbearing potential (i.e., any female who is post-menopausal [greater than 1 year without menstrual period in the absence of hormone replacement therapy]) or surgically sterile; or,
b) If pre-menopausal or menopausal for 1 year or less, must have a negative pregnancy test and must not be lactating at Screening. Female subjects of childbearing potential and who are sexually active are required to practice highly effective methods of birth control. Female subjects for whom menopausal status is in doubt, in the opinion of the investigator, will be

required to use a highly form of birth control.
Highly effective forms of birth control are defined as methods that have a failure rate of less than 1% per year when used correctly and consistently and include:
• combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation; oral, intravaginal, or transdermal
• progestogen-only hormonal contraception associated with inhibition of ovulation; oral, injectable, or implantable
• intrauterine device (IUD)
• intrauterine hormone-releasing system (IUS)
• bilateral tubal occlusion
• vasectomised partner
• sexual abstinence
•Double barrier method
6) Subject has the ability to comply with procedures for cognitive and other testing in the opinion of the investigator.
7) Subject must be able to ingest pills (in tablet form) whole.
8) Subject lives with (or has substantial periods of contact with) a regular caregiver who is willing to attend visits, oversee the subject's compliance with protocol-specified procedures and study medication, and report on subject's status, and who has substantial contact with the subject. If the caregiver does not cohabitate with the subject, he/she ideally should have a minimum of 10 hours total and at least 3 days contact with the subject per week. Prior to randomization, study staff will review eligibility of non-cohabitating caregivers. Every effort should be made to have the same caregiver throughout the study.
10) Subject has provided 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 (LAR) has provided full written informed consent on behalf of the subject.
11) Caregiver has provided full written informed consent on his/her own behalf prior to the performance of any protocol-specified procedure.
12) The subject*s general health status is acceptable for participation in a 24-week study in the opinion of the investigator.

Exclusion criteria

Other Causes for Dementia : ;1) Parkinson*s disease dementia, vascular dementia, frontotemporal dementia, or Alzheimer*s disease dementia.
2) A CT or MRI scan performed within the past 12 months or at Screening could be interpreted as the
primary cause of dementia (e.g., cerebrovascular disease [transient ischemic attack, stroke, hemorrhage]; structural or developmental abnormality; epilepsy; infectious, or degenerative or inflammatory/demyelinating CNS conditions) or any other history and/or evidence to suggest the same.
3) Current vitamin B12 deficiency, hypothyroidism, neurosyphilis, HIV dementia, or Korsakoff*s encephalopathy.
4) Focal findings on the neruological exam ;Confounding Medical Conditions:;5) History of

schizophrenia, major depressive episode in the past 6 months bipolar affective disorder that in the opinion of the
investigator would interfere with participation in the study or could affect performance on outcome measures.
6) Significant suicide risk as defined by (1) suicidal ideation as endorsed on items 4 or 5 on the C-SSRS within the past year, at Screening or at Baseline or; (2) suicidal behaviors within the past year or; (3) clinical assessment of significant suicidal risk during subject interview.
7) History of epilepsy, unexplained seizure or history of significant head trauma with loss of consciousness in the past 5 years.
8) History of malignancy during the 5 years before Screening. History of basal cell carcinoma and melanoma in situ are permitted. History of other cancers currently in a non-active state may be acceptable after review with the Medical Monitor.
9) Any clinically relevant concomitant disease including unregulated diabetes, progressive liver or kidney dysfunction, history of myocardial infarction or unstable angina within 6 months of Screening, history of more than one myocardial infarction within 5 years of Screening, history of clinically significant stroke, or any other medical or psychiatric condition, which, in the opinion of the investigator, makes the subject unsuitable for inclusion in the study.
10) History of alcohol use disorder or other substance abuse disorder (excluding tobacco use).;Concomintant Medications:;11) Participation in another investigational drug or device study during the 30 days prior to the Screening Visit (Visit 1), or within 5 half-lives of use of the investigational drug prior to the Screening Visit, whichever is longer.
12) Treatment with any concomitant medications : Butyrophenones, phenothiazines, and other *conventional* antipsychotics, Barbiturates, MAO inhibitors, Any investigational drug, warfarin, phenytoin and phenprocoumon, (R)-acenocoumarol, ketoconazole, itraconazole, erythromycin,
rifampicin, phenytoin and carbamazepine, itraconazole, ketoconazole, cyclosporin, diltiazem, verapamil, quinidine, and carvedilol.;Unacceptable Tests/Laboratory values: ;13) Alanine transaminase (ALT) and/or aspartate aminotransferase (AST) >=2.0 times upper limit of normal (ULN) at Screening.;14) Total bilirubin over 1.5 x ULN at Screening except due to documented Gilbert*s disease or evidence of Gilbert*s disease on Screening laboratory assessments.;15) Calculated creatinine clearance <40 mL/min (Cockroft-Gault formula) at Screening:
16) Positive hepatitis B surface antigen or hepatitis C antibody test at Screening.;17) Confirmed corrected QT interval (QTc) value greater than or equal to 450 msec for males or greater than or equal to 470 msec for females at Screening.

Study design

Design

Study phase:	2
Study type:	Observational invasive

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	02-01-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RVT-101
Generic name:	RVT-101

Ethics review

Approved WMO Date:	25-04-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	12-08-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-11-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	14-12-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-01-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-005495-19-NL
ClinicalTrials.gov	NCT02669433
CCMO	NL57266.056.16

Study results

Date completed: 04-12-2017

Results posted: 22-08-2019

First publication
15-02-2019