A 26- week Extension study of the safety and clinical effects of EVP-6124 in subjects with Alzheimer's disease currently or previously receiving an acetylcholinesterase inhibitor medication

Published: 21-08-2014
Last updated: 20-04-2024

Primary ObjectivesTo assess the safety of 2 fixed doses of EVP-6124 (2 or 3 mg daily) for up to 52 weeks in subjects withAlzheimer*s disease (AD) who complete (Day 182) studies EVP-6124-024 or EVP-6124-025Secondary ObjectivesTo assess the duration...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON41994

Source
ToetsingOnline

Brief title
EVP-6124-026

Condition

- Neurological disorders NEC

Synonym
Dementia and Alzheimer's disease

Research involving
Human

Sponsors and support

Primary sponsor: Forum Pharmaceuticals, Inc
Source(s) of monetary or material Support: Envivo pharmaceuticals

Intervention

Keyword: Alzheimer's disease, EVP-6124, extension study, phase 3

Outcome measures

Primary outcome

Safety Outcomes: Frequency of treatment-emergent AEs (TEAEs), serious TEAEs, related TEAEs, and TEAEs that result in study drug discontinuation will be evaluated. Descriptive statistics for the change from baseline in vital sign measurements, physical examinations, laboratory test results for hematology and chemistry, 12-lead ECGs, C-SSRS and GDS will be assessed over time. An interim analysis for safety reporting may be performed when a sufficient number of subjects have completed 52 weeks of EVP-6124 treatment. Investigators and study staff will remain blinded to the dose assignment for the previous study.

Clinical Effects Outcomes: Descriptive statistics to assess the change from baseline in the MMSE, NPI, ZBI, and EQ-5D results over time will be presented; results of the RUD-Lite© 3.3 over time will also be presented.

A statistical analysis plan will be finalized before the database is locked to

document the detailed analysis

methods, data handling procedures, and other statistical analysis issues.

Secondary outcome

na

Study description

Background summary

Alzheimer*s disease (AD) is the leading cause of dementia in the elderly. The prevalence of dementia in those >=65 years
in North America is approximately 6 to 10%, with AD accounting for approximately 66% of these cases. This illness
represents a steadily growing medical and social problem of our aging societies, with an overall prevalence rate of 8.3
million patients in 7 countries. As the population ages, the burden of AD is expected to grow substantially in upcoming
decades.
Improvements for behavioral symptoms, which often are a major factor increasing caregiver burden, are rather low.
Therefore, more efficacious drugs are urgently needed to improve the treatment of cognitive deficits in patients with AD.
Studies in both neurochemical and animal-behavioral models indicate that nicotinic acetylcholine receptor agonists may
be useful for the treatment of cognitive deficiencies in subjects with mild to moderate dementia due to AD.
EVP-6124 is a potent agonist of the α7 nicotinic acetylcholine receptor (nAChR), which is located in several brain areas
involved in cognition and memory, such as the cerebral cortex and the hippocampus.
Overall, this study design addresses key clinical and scientific areas of interest in cognitive impairments, activities of daily
living, psychiatric and behavioral symptoms, caregiver burden, quality of life, and pharmacoeconomic outcomes
associated with mild to moderate dementia due to AD and attempts to gain further understanding of the effects and safety of EVP6124
in the study population.

Study objective

Primary Objectives
To assess the safety of 2 fixed doses of EVP-6124 (2 or 3 mg daily) for up to 52 weeks in subjects with
Alzheimer*s disease (AD) who complete (Day 182) studies EVP-6124-024 or EVP-6124-025
Secondary Objectives
To assess the duration of clinical effects of EVP-6124 for up to 52 weeks on the following endpoints:
• Cognition using the Mini-Mental State Examination (MMSE)
• Psychiatric and behavioral symptoms using the Neuropsychiatric Inventory (NPI)
• Quality of life using the EuroQol-5D* (EQ-5D), pharmacoeconomic outcomes using the Resource
Utilization in Dementia (RUD-Lite©3.3), and caregiver perceived burden using the Zarit Burden Interview (ZBI)

Study design

This is a 26-week, randomized extension of the Phase 3 double-blind placebo-controlled studies, EVP-6124-024
and EVP-6124-025. In these studies, subjects diagnosed with mild to moderate dementia due to AD currently
or previously treated with an acetylcholinesterase inhibitor (AChEI) (donepezil, rivastigmine, or galantamine)
received EVP-6124 (2 or 3 mg daily) or placebo for 26 weeks.
In this extension study, subjects who complete study EVP-6124-024 or EVP-6124-025 (Day 182) and fulfill all
entry criteria will be randomized to receive EVP-6124 2 or 3 mg daily for 26 weeks (182 days). The term
randomized will refer to all subjects, including subjects previously treated with EVP-6124 who will receive
the same dose during this study as received in the previous study and subjects previously treated with placebo
who will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio). Subjects, investigators and study staff will
remain blinded to the EVP-6124 dose assignment for all subjects. Assessments performed at the final
double-blind study visit (Day 182) will serve as the baseline for this extension study for all subjects. Subjects
who do not immediately elect to enroll in the extension study on Day 182 must do so within 5 days to be
eligible for study entry.
During this extension, subjects receiving an AChEI may continue these medications and dose changes are
allowed, and subjects not receiving an AChEI may have AChEI treatment re-initiated.
Each subject is required to have a reliable and capable support person/caregiver who interacts with the subject

approximately 4 times per week and will be available to attend clinic visits in person when possible.

Intervention

subjects previously treated with EVP-6124 in the EVP-6124=-015 study,will receivethe same dose during this study as received in the previous study (2 or 3 mg) and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

Study burden and risks

The patient will be in the study for 27 weeks which will involve a minimum of 6 visits to the site. Each visit will last between 1-3 hours. Also, the patient will be contacted by phone in between visits.

During the visits in the clinic, physical examinations will be done (6x) directed to constipation and other GI related AEs, vitals will be taken, weight will be measured. Blood draw (6 visits approx 12 ml per visit), and ECG will be done during 5 visits. Women of childbearing potential will have a urine pregnancy test(6x). A certified rater will perform the following tests: Colombia-Suicide Severity rating Scale (C-SSRS 6x) and Geriatric Depression scale (GDS 2x)

The following cognitive assessments will be done: Mini-mental state examination (MMSE 2x).
Funcional and behavioral assesments will be done: Neuropsychiatric Inventory (NPI 2x)
pharmaco-economics, caregiver perceived burden and quality of life will be measured through: Resource Utilization in Demetia (RUD-Lite© 3.3 2x), Zarit Burden Interview (ZBI 32x), EQ-5D 2x
During this extension stud, the patient will have weekly calls during the first 8 weeks to assess constipation and other GI-related events. These calls will be every other week after 8 weeks , as well as on day189 (end of treatment) and 30 days after the last dose in case of an SAE.

Across completed studies, the most commonly experienced treatment emergency adverse events were constipation (6.8%, EVP-6124;0.9%, placebo) and headache (6.9%, EVP-6124;5.9%, placebo); these events were generally mild, transient, and usually resolved without treatment.
Mental function (thinking, concentrration, memory)of an individual may or may not improve while particiapting in this study. Partiicpation in this studywill provide scientific information on safety of EVP-6124, but also on the efficacy of EVP-6124 on the mental function in the human brain. This information is useful for a larger population where cognitive impairment could occur such as

Alzheimer's disease.

Contacts

Public
Forum Pharmaceuticals, Inc

Arsenal street 500
Watertown MA 02472
US
Scientific
Forum Pharmaceuticals, Inc

Arsenal street 500
Watertown MA 02472
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Informed consent form (ICF) for this extension study signed by the subject or legally acceptable
representative and an ICF signed by the support person/caregiver before initiation of any study-specific
extension procedures
2. Successful completion (Day 182) of study EVP-6124-024 or EVP-6124-025
3. No clinically significant change in the judgment of the investigator in the subject*s medical status during study EVP-6124-024 or EVP-6124-025
4. In the judgment of the investigator, extension treatment is in the best interest of the

subject
5. Fertile, sexually active subjects (men and women) must use an effective method of contraception during the study. Female subjects and the female partner of male subjects must be surgically sterile (hysterectomy or bilateral tubal ligation), postmenopausal for at least 1-year, or willing to practice adequate methods of contraception if of childbearing potential (defined as consistent use of combined effective methods of contraception [including at least 1 barrier method])
6. Reliable and capable support person/caregiver, who if not living in the same household, interacts with the subject approximately 4 times per week and will be available to attend clinic visits in person when possible

Exclusion criteria

1. Significant risk of suicidal or violent behavior in the judgment of the investigator
2. Adverse events (AEs) from the previous study (EVP-6124-024 or EVP-6124-025) that have not resolved,are moderate or severe, judged to be possibly related or related to study drug, and considered by the investigator to be a contraindication to extension study participation
3. Any condition that would make the subject in the judgment of the investigator unsuitable for the study
4. Female subjects who are pregnant, nursing, or planning to become pregnant during the extension study

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	EVP-6124
Generic name:	EVP-6124

Ethics review

Approved WMO Date:	21-08-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-12-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-04-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-11-2015
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	EUCTR2013-002654-75-NL
CCMO	NL48763.056.14