

1.5 versus 3.0 mg APL510 to normalise sleep patterns in elderly subjects with insomnia

Submission date 15/01/2010	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 15/01/2010	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 24/05/2016	Condition category Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Public

Contact name
Ms Rebecca Scoble

Contact details
Alliance Pharmaceuticals Ltd
Avonbridge House
Bath Road
Chippenham
United Kingdom
SN15 2BB
+44 1249 466966
medinfo@alliancepharma.co.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
APL510-008

Study information

Scientific Title

A double-blind placebo controlled crossover study to determine if 1.5 and 3.0 mg of APL510 can normalise sleep patterns in elderly subjects with difficulty in maintenance of sleep and/or initiating sleep onset

Study objectives

The primary objective was to determine the efficacy of 1.5 and 3.0 mg of APL510 in the management of insomnia defined as self-reported poor sleep quality, in the elderly. The secondary objectives were to determine the safety profile of APL510 and to determine the ease of withdrawal of APL510. The tertiary objective was the evaluation of the quality of life (QoL) of subjects throughout the study using the 36-item Short Form (SF-36) QoL assessment and the EuroQoL assessment (EQ-5D) questionnaire.

The trial was previously registered at Pharmaceutical Industry Clinical Trials Database (ABPI /CMR) - <https://www.cmrinteract.com/clintrial/default.htm>.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Fife and Forth Valley local research ethics committee, 03/03/2005 (ref: 05/S0501/19)

Study design

Double-blind placebo-controlled randomised cross-over study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

GP practice

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Insomnia

Interventions

This was a double-blind, placebo-controlled, randomised, cross-over study of a sustained release formulation of melatonin, APL510, at doses of APL510 1.5 mg and APL510 3.0 mg. It was planned that a total of 26 matched pairs were required for the efficacy analysis. Therefore, in order to reach this number of completed subjects, a total of up to 80 could be recruited, to allow for dropouts.

Subjects had a 2-week treatment-free period run-in to assess their suitability for inclusion. All subjects were then randomised to receive the following active and placebo treatments for a period of 4 weeks, each separated by a 1-week treatment-free period:

1. APL510 1.5 mg followed by placebo followed by APL510 3.0 mg
2. APL510 3.0 mg followed by APL510 1.5 mg followed by placebo
3. Placebo followed by APL510 3.0 mg followed by APL510 1.5 mg

Ease of withdrawal was assessed at the end of each treatment sequence, not each period. In addition, the number of night-time awakenings was not included in the updated version of the diary introduced during the study and only 50% of subjects were randomised to actigraphy.

Scientific Contact Details - Lead Principal Investigator:
Dr Douglas McKeith, MB ChB BSc MRCGP DRCOG DCCH
Formerly of Synergie Consultancy Limited
Unit 6.07 Kelvin Campus
West of Scotland Science Park
Glasgow, G20 0SP
United Kingdom

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

APL510

Primary outcome measure

Total sleep time of subjects as recorded in sleep diaries. The primary comparison for efficacy was the average of the primary outcomes under the two APL510 doses (1.5 mg and 3 mg) versus placebo.

Measured throughout the study and the data was averaged or tabulated after completion of the study.

Secondary outcome measures

Secondary measures of efficacy revolved largely around the subjective scales employed. These were as follows:

1. Time to sleep onset
2. Number of night-time awakenings
3. Ease of getting to sleep
4. Sleep quality
5. Ease of awakening
6. Behaviour following waking

Measured throughout the study and the data was averaged or tabulated after completion of the study.

Overall study start date

23/07/2005

Completion date

24/11/2006

Eligibility

Key inclusion criteria

1. Male or female subjects aged 65 years or more presenting with self-reported poor sleep quality defined as at least two of the following:
 - 1.1. Regularly took more than 45 minutes to fall asleep (at least three nights per week)
 - 1.2. Overall night-time sleep less than 5 hours on at least 3 nights per week
 - 1.3. Regular night-time awakenings defined as at least twice per night on at least 3 nights per week
2. Subjects with a poor sleep quality for at least 8 weeks
3. Written informed consent

Participant type(s)

Patient

Age group

Senior

Sex

Both

Target number of participants

Up to 80 participants

Key exclusion criteria

1. Had a clinically significant unstable medical abnormality, chronic disease or history or presence of significant neurological, hepatic, renal, endocrine, cardiovascular, gastrointestinal, pulmonary, psychiatric, metabolic disease or malignancy which in the opinion of the investigator would have precluded successful participation in the study
2. Had a recent history of (less than 2 years) alcohol or drug abuse or current evidence of substance dependence or abuse as defined by the Diagnostic and Statistical Manual of Mental Disorders-IV criteria
3. Had major depression or anxiety causing sleep disturbance as defined by Diagnostic and Statistical Manual of Mental Disorders-IV criteria
4. Had a clinically significant illness within the last 30 days
5. Routine biochemistry parameters (e.g., creatinine or liver function tests) greater than 2 x the upper limit of normal for this age of population. Haemoglobin less than 10 g/dL.
6. Subjects receiving B6 or B12 supplements (multivitamin supplements were allowable provided intake did not exceed the recommended daily dose)
7. Subjects receiving warfarin or other vitamin K antagonists
8. Subjects planning to travel through more than two time zones whilst entered into the study
9. Subjects with a known hypersensitivity to melatonin or any of the excipients in the formulation
10. Subjects who, by virtue of the need to care for a close family member, were subjected to intermittent night-time disturbance
11. Subjects who had experienced the bereavement of a close family member within the last 3 months
12. Subjects who had used any other investigational drug within the last 30 days

13. Subjects planning to work night shifts

14. Subjects on treatment with anxiolytics, antidepressants, anticonvulsants, hypnotics or strong narcotic analgesics within the last 30 days. Other narcotic analgesics were allowed if they had been used at a constant dose for at least the last 30 days, the dose was unlikely to change during the duration of the study and in the opinion of the investigator, not likely to interfere with the subject's sleep quality. Subjects receiving hypnotics were eligible for the study if they consented to withdraw from treatment for 16 days prior to screening.

15. Subjects with a known severe allergic or auto-immune disease

16. Subjects with other conditions that may have caused night-time awakenings (e.g., nocturia or uncontrolled nocturnal pain) that in the investigator's opinion would have interfered with the assessment of the subject's sleep disturbance

17. Subjects who, in the opinion of the investigator, were unlikely to complete the study satisfactorily

Subjects were advised that caution was to be exercised when driving or operating any heavy or dangerous machinery within 6 hours of taking a dose of study medication.

Date of first enrolment

23/07/2005

Date of final enrolment

24/11/2006

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Alliance Pharmaceuticals Ltd

Chippenham

United Kingdom

SN15 2BB

Sponsor information

Organisation

Alliance Pharmaceuticals Ltd (UK)

Sponsor details

Avonbridge House

Bath Road

Chippenham

United Kingdom

SN15 2BB
+44 (0)1249 466966
info@alliancepharma.co.uk

Sponsor type
Industry

Website
<http://www.alliancepharma.co.uk>

ROR
<https://ror.org/001zd1d95>

Funder(s)

Funder type
Industry

Funder Name
Alliance Pharmaceuticals Ltd (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration