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

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
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

Study type(s)
Treatment

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.

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Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
APL510

Primary outcome(s)
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.

Key secondary outcome(s))
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 wakening

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

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

Healthy volunteers allowed
No

Age group
Senior

Sex
All

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
United Kingdom

England

Study participating centre
Alliance Pharmaceuticals Ltd
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Sponsor information

Organisation
Alliance Pharmaceuticals Ltd (UK)

ROR
https://ror.org/001zd1d95

Funder(s)

Funder type
Industry

Funder Name
Alliance Pharmaceuticals Ltd (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration