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The use of APL510 to improve the length of day time sleep in subjects working permanent night-shifts

Submission date
15/01/2010

Recruitment status
No longer recruiting

Registration date
15/01/2010

Overall study status
Completed

Last Edited
21/06/2016

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
APL510-009

Study information

Scientific Title

A double-blind placebo controlled crossover study to determine if melatonin can improve the length of day time sleep in subjects with transient misalignment of the sleep-wake cycle as a result of working permanent night-shifts

Study objectives
The primary objective was to determine if APL510 tablets (containing 1.5 mg of melatonin) increased the length of daytime sleep following a night-shift.

The secondary objectives were:
1. To determine if APL510 tablets increased the maintenance of daytime sleep and reduced sleep latency and the number of episodes of disturbed sleep following a night-shift
2. To determine if APL510 had any 'residual' effect during the night-shift work period
3. To compare the adverse event (AE) profiles of APL510 and placebo

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)
South Birmingham Research Ethics Committee, 04/04/2005, ref: 05/Q2707/56

Study design
Single centre double-blind placebo-controlled two-way crossover study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Insomnia

Interventions
This was a single centre, double-blind, placebo-controlled, two-way crossover study. Subjects included in the study worked one of two shift patterns: 4 nights working followed by 4 nights not working ("4 nights on, 4 nights off") and 3 nights working followed by 4 nights not working ("3 nights on, 4 nights off").

Subjects were randomised to one of two treatment sequences: either placebo followed by APL510 1.5 mg or APL510 1.5 mg followed by placebo. Subjects took study medication for one work shift period and then crossed over to the next randomised treatment. Subjects attended their final visit at the end of their second treatment period, although a further follow-up visit was available during the next work shift period for subjects who had ongoing adverse events (AEs) at the end of the second treatment period.

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Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Mean total sleep time over the days on which diary entries were recorded.

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

Key secondary outcome(s))
1. Mean number of daytime awakenings
2. Potential hangover effects

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

Completion date
19/04/2006

Eligibility

Key inclusion criteria
1. Male or female subjects aged 18 to 65 years working permanent night-shifts with at least three consecutive night-shifts in their shift pattern
2. A female subject could be included if:
2.1. She was of non-child-bearing potential (e.g., post-menopausal for 1 year, had undergone bilateral tubal ligation, had undergone a hysterectomy or was physiologically incapable of becoming pregnant), or
2.2. She was of childbearing potential practising an acceptable method of birth control defined as the use of oral or depot hormonal contraception, an intrauterine contraceptive device or a combination of both spermicidal and barrier methods of contraception (a partner having had a vasectomy was not an acceptable reason for inclusion), or
2.3. Total abstinence from sexual intercourse was maintained
3. Provided written informed consent
4. No planned absences from work, other than rest days, for the duration the subject was in the study. Subjects could work additional night-shifts as overtime

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. 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 or other clinically relevant abnormality which in the opinion of the Investigator would preclude successful participation in the study
2. A recent history (less than 2 years) of alcohol or drug abuse or current evidence of substance dependence or abuse as defined by Diagnostic and Statistical Manual of Mental Disorders-IV criteria, with the exception of nicotine dependence
3. Female subjects who were pregnant, not using an adequate form of contraception or breast-feeding
4. Subjects receiving vitamins B6 and B12 supplements (excluding multivitamin supplements at recommended dose)
5. Subjects with a known hypersensitivity to melatonin or any of the excipients in the formulation
6. Subjects receiving hypnotics, tricyclic antidepressants, monoamine oxidase inhibitors, serotonin reuptake inhibitors, lithium, beta-blockers, calcium channel blockers, central alpha-blockers, non-steroidal anti-inflammatory drugs (excluding occasional over-the-counter use), alprazolam, triazolam, neuroleptics, or barbiturates. Subjects receiving any of these compounds were eligible for entry provided the medication was stopped 2 weeks prior to study entry.
7. Subjects with a known history of impaired hepatic or renal function defined as transaminases greater than 2 x the upper limit of normal or creatinine clearance of less than 35 mL/min
8. Subjects with a known severe allergic or auto-immune disease (e.g., multiple sclerosis, rheumatoid arthritis, severe asthma and systemic lupus erythematosus)
9. Subjects who had received an experimental drug within the previous 3 months
10. Subjects using melatonin
11. Subjects, who, by virtue of the need to care for close family members, might have been subjected to intermittent disturbance during their daytime rest periods
12. Subjects who, in the opinion of the Investigator, were not capable of completing the study
13. Subjects who did not consent to their General Practitioner being informed of their participation in the study

Pregnant or breast feeding women were excluded as the preclinical data on melatonin in this group were not available at the start of the study. Subjects were advised that caution should 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
10/10/2005

Date of final enrolment
19/04/2006

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