AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not Applicable
ACTIVE INGREDIENT: Donepezil 5mg, followed by 10mg

Study No: D2285M00010
A Randomised, Double-blind, Placebo-controlled, Parallel Design, Multicentre Study in Patients With Mild to Moderate Alzheimer's Disease to Investigate the Effect on Cognitive Function as Measured by Repeated CogState Testing in Relation to Effects on Traditional Cognitive Measures After 12 Weeks

Developmental Phase: 0
Study Completion Date: January 2011
Date of Report: 23 May 2011

OBJECTIVES:

The primary objective was to evaluate the efficacy of donepezil in improving cognitive function at 4 weeks using repeated measures methodology and the CogState test battery, as compared to placebo.

Secondary objectives:

- Evaluate whether, CogState effect observed early (i.e. at 4 weeks) were predictive of ADAS-COG and /or NTB at 12 weeks.
- Evaluate the optimal number and interval of measurements during pre-dose and treatment period and length of treatment needed to detect an effect with CogState.
- Assess effects on cognition of donepezil compared to placebo in change from baseline on the Alzheimer's Disease Cooperative Study – Clinical Global Impression of Change (ADCS-CGIC) and the Mini Mental State Exam (MMSE).

METHODS:

Selected tasks from the CogState computerized cognitive battery which have demonstrated rapid sensitivity to cognitive effects of drugs, were administered for 10 different days within a two week period prior to treatment, and then on five occasions at one month intervals during three months of treatment with donepezil (5mg for two weeks, then 10mg) or placebo.

Cognitive function was also assessed by using the original 11-item version of Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog) (Rosen et al 1984).

Cognitive function was assessed by using the original 9-item version of the Neuropsychological Test Battery (NTB) (Harrison et al 2007).

ADAS-Cog and NTB were administered two weeks prior to randomization, and then on different days at baseline and at monthly intervals.

The Alzheimer's disease Cooperative Study – Clinical Global Impression of Change (ADCS-CGIC) is a standardised method for making CGIC ratings in patients with Alzheimer's disease (Schneider et al 1997).

Cognitive function and eligibility was assessed by using the Mini Mental State Exam (MMSE)

RESULTS:

The primary objective was not met since the composite CogState test battery did not differentiate donepezil from placebo at 4 weeks when averaging all 10 baseline and all 5 follow up assessments.

The predictability of the composite CogState test battery score at 4 weeks for an effect of donepezil versus placebo on ADAS-Cog at NTB global composite scores at 12 weeks could not be addressed due to lack of effects on all measures at these time-points.

Evaluation of the optimal number and interval of CogState measurements during pre-dose and treatment period showed that no significant effect of donepezil could be detected at four weeks even after dropping leading measurements or terminal measurements.

Adverse Events (AEs) were more common in the donepezil group (101 AEs in 37 patients) as compared to the placebo group (52 AEs in 26 patients). Most common AEs were typical for donepezil treatment. There were no AEs leading to death.

Three Serious Adverse Events were seen in 2 patients and Discontinued Adverse Events (DAE) were more common in the donepezil group (8 patients) as compared to the placebo group (1 patient). Most DAEs occurred during the first 4 weeks.

No apparent effects on blood laboratory values, urinalysis or vital signs