Studie 037

(M20200037)

Results only report

Clinical Study Report: Protocol A5981027 (M20200037)

Protocol Title: Efficacy and Safety of Reboxetine vs Fluoxetine in the Treatment of Outpatients With Single or Recurrent Major Depressive Episodes

Investigators: Available on request.

Study Centres: Available on request.

Publications Based on the Study: None

Study Objectives:

- To determine the clinical efficacy of reboxetine compared to fluoxetine in subjects diagnosed with an episode of major depression, with or without previous treatment
- To compare the safety profile of both drugs

INTRODUCTION

Major depression is defined as a depressive mood experienced daily and lasting for at least 2 weeks. An episode may be characterised by sadness, indifference or apathy or irritability, and is usually associated with a change in a number of neurovegetative functions, including sleep and weight patterns, agitation or motor retardation, fatigue, difficulty in concentration and decisions, shame or guilty feelings and death or suicide ideas. Currently there are 5 generations of antidepressants for the treatment of major depression.

Fluoxetine and reboxetine were used in this study. Fluoxetine, a non-tricyclic antidepressant, is a selective serotonin reuptake inhibitor which is effective in the management of psychogenic depressions. Fluoxetine also blocks muscle receptors and neuronal nicotinic acetylcholine receptors. Neuronal nicotinic acetylcholine receptors are widely distributed throughout the central nervous system and peripheral nervous system and the blocking action of fluoxetine on these receptors may play a role in its therapeutic effects. Reboxetine is also a potent antidepressant. Reboxetine is a selective noradrenaline reuptake inhibitor with low affinity for alpha-adrenergic and muscarinic receptors.

Clinical efficacy of both fluoxetine and reboxetine has been measured for remission rates of depression. Reboxetine has been observed to have a higher effect upon the readapting of the individual to everyday life and to his regular activities. If reboxetine can improve the social readapting of depressed patients with remission, a number of years of incapacity and suffering among these patients could be avoided.

METHODS

Study Design: This was a 12-week, randomised, open-label, multi-centre study with parallel groups comparing the efficacy, tolerance and safety of reboxetine vs fluoxetine in the remission rates of depression and readapting of subjects with major depression. The study planned to

enroll 120 subjects in a total of 10 health centres. Subjects were randomised to 2 treatment arms. After a 7 day wash out period at the start of the study, subjects were administered either reboxetine (8 mg/day) or fluoxetine (20 mg/day). The dose of reboxetine and fluoxetine was increased to 10 mg/day and 40 mg/day, respectively, at the end of the fourth week.

Diagnosis and Main Criteria for Inclusion: Male and female outpatients aged between 18 and 65 years with major depression according to the criteria addressed in Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV), without psychotic data for at least 2 weeks of depressive symptoms and with a score of ≥ 18 points for Hamilton Depression Rating Scale (HDRS or HAM-D) for the first 17 of 27 items were enrolled in the study.

Study Treatment: Subjects were randomised either to reboxetine 8 mg/day or fluoxetine 20 mg/day after receiving placebo for a washout period for 7 days at the start of the study. The dose of reboxetine and fluoxetine was increased to 10 mg/day and 40 mg/day, respectively, at the end of the fourth week.

Efficacy Evaluations: Psychiatric evaluations with efficiency evaluating scales (Montgomery-Asberg Rating Depression Scale, HDRS, Beck Depression Inventory, Global Clinical Impressions, Self-Assessment of Social Adaptation Scale) were conducted at the start of the study and at Weeks 1, 2, 4, 6, 8 and 12**.**

Safety Evaluations: Safety assessments included recording of adverse events (AEs) and serious adverse events throughout the study. A complete physical examination was conducted at the start of the study and at Weeks 1, 2, 4, 6, 8 and 12. Laboratory tests (blood count and blood chemistry) were conducted at the start of the study and at Week 12.

Statistical Methods: Efficacy analyses included subjects who had received study drug for at least 3 weeks and had 4 evaluations, including a baseline evaluation. A variance analysis was performed to determine the mean and standard deviation for each of the depression scales, at the start of the study and at the end of treatment for each treatment arm and between the 2 treatment arms. A gross analysis was conducted to determine the association between clinical scales and the social adaptation scale.

Safety analyses included subjects who had received at least 1 dose of study drug. Safety and tolerance was assessed by spontaneously reported AEs.

RESULTS

Safety Results:

Deaths and Serious Adverse Events:

Table S1 Serious Adverse Events

Subject ID	Sex/Age	MedDRA Preferred Term	Total Daily Dose	Investigator Causality	Clinical Outcome
Study Drug: Reboxetine					
M20200037\28	F/36 years	Suicidal ideation	16 mg	Other	Recovered
M20200037\72[a]	M/65 years	Erectile dysfunction	8 mg	Study drug	Recovered
M20200037\97[a]	M/33 years	Constipation	10 mg	Study drug	Not recovered

Source: Table 13.6.5
ID = Identifier; M = Male; F = Female
[a] Subject permanently discontinued from the study
MedDRA- Medical Dictionary for Regulatory Activities v10.1

As of 03 April 2008 there was no entry in Pfizer's Safety Database for deaths for protocol A5981027 (M20200037).

Date of Report: 14 January 2009