A Phase III Prospective Active and Placebo- Controlled Randomized Trial of Vilazodone in the Treatment of Major Depressive Disorder

Abstract

Background

Depression is a leading cause of psychiatric morbidity in the modern world, and the introduction of selective serotonin reuptake inhibitors (SSRIs) is a revolution in the treatment of depression. Major depressive disorder (MDD) is a prevalent psychiatric ailment worldwide, affecting more than 350 million people of all ages. Over 30% of patients with MDD do not achieve an adequate response and remission after treatment. Non-adherence and premature treatment discontinuation are common and can be traced back to limited efficacy or delayed onset as well as intolerable adverse events, especially weight gain and sexual dysfunction. SSRIs are the most commonly prescribed first-line antidepressants for the treatment of MDD. Vilazodone, a novel SSRI and 5-HT_{1A} partial agonist received FDA approval in 2011 to treat the major depressive disorder (MDD) in adults. This Phase III study conducted in India aimed to evaluate the efficacy and safety of vilazodone when compared to escitalopram or placebo in patients with MDD.

Methods

This was a prospective, multicentre, randomized, comparative study of 375 participants over eight weeks of treatment with either vilazodone (10-40mg/day) or escitalopram (10-40 mg/day) or placebo in adult patients with MDD. Primary efficacy was assessed using the Hamilton Rating Scale for Depression (HAM-D-17); secondary efficacy was assessed using the Montgomery-Asberg Depression Rating Scale (MADRS) score and Hamilton Anxiety Scale (HAM-A) score. Safety parameters included adverse events (AEs), clinical laboratory results, vital signs, electrocardiogram (ECG), and Columbia-Suicide Severity Rating Scale (C-SSRS).

Results

Mean change in the HAM-D-17 total score from baseline to week 8 for vilazodone, escitalopram, and placebo-treated patients in intent-to-treat (ITT) population was: -18.9 (± 7.49), -17.8 (± 6.06), and -7.4 (± 6.32); in ITT population (with Last Observation Carried Forward(LOCF) imputation) was: -17.9 (± 7.71), - 17.4 (± 6.19), and -6.4 (± 6.84), and in per-protocol (PP) population was: -19.1 (± 7.20), -17.8 (± 6.08), and -7.7 (± 6.29), respectively. The upper limit of 95% CI (0.56 (ITT); 0.90 (ITT with LOCF Imputation); 0.23 (PP)) of

difference in HAM-D-17 between vilazodone 40mg and escitalopram 40mg, which is lower than the defined non-inferiority margin (3.56), proving non-inferiority. The difference between vilazodone 40mg, escitalopram 40mg, and the placebo was statistically significant ($p<0.0001$). No deaths or serious adverse events were reported in this study.

Conclusion

Vilazodone demonstrated comparable efficacy to escitalopram and superior efficacy over the placebo in the treatment of MDD.