The treatment responses to standard-of-care (oral daily) antidepressants remain suboptimal 79 (29.5) 58 (21.6) 26.8 (2.6) 39.4 (12.3) 206 (76.6) 8 (3.0) 4 (1.5) 76 (28.3) 1 (0.4)

Dysregulated gamma-aminobutyric acid (GABA) signaling may contribute to the For all subgroups examined based on baseline demographics and clinical

Introduction

Robert Lasser, MD, MBA, 1 Anita H Clayton, MD, 2 JungAh Jung, PhD, 1 Colville Brown, MD, 1 Stephen J Kanes, MD, PhD, 1 James Doherty, PhD 1

Objective: To evaluate the safety and tolerability of zuranolone in treatment-resistant major depressive disorder (MDD) patients in a 2-week, double-blind, placebo-controlled study. Methods: This was a phase 3, multicenter, randomized, double-blind, placebo-controlled study of zuranolone (50 mg once daily) in patients with treatment-resistant MDD (primary endpoint: change from baseline in HAMD-17 total score at Day 15). Results: A total of 327 patients were randomized to receive zuranolone (n = 164) or placebo (n = 163). Baseline demographics and clinical characteristics were generally well balanced, except a higher MI score in the placebo group. At Day 15, the least-squares mean (95% confidence interval) change from baseline in HAMD-17 total score was -5.64 (-7.21, -4.07) for zuranolone and -0.87 (-2.43, 0.70) for placebo (p = 0.0019). There were no significant differences in treatment-emergent adverse events or other adverse events in any treatment group. Conclusions: Zuranolone was well tolerated in patients with treatment-resistant MDD. Clinical trial registration number: NCT04464768. 1 Sage Therapeutics, Inc., Cambridge, MA; 2 University of Virginia, School of Medicine, Charlottesville, VA.