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Efficacy and safety of zuranolone in major depressive disorder and postpartum depression: A meta-analysis of meta-regression and dose-response analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202360087

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 June 2023 and was last updated on 28 June 2023.

INTRODUCTION

Review question / Objective PICO question was (1) population: people with diagnosis of major depressive disorder; (2) intervention: full course of zuranolone regimen; (3) comparison: placebo; (4) outcome: changes in depression and anxiety severity, as well as dropout and side effect rateschange in severity of depression.

Condition being studied Zuranolone, also known as SAGE-217, is a synthetic neurosteroid being developed as a potential treatment for major depressive disorder and postpartum depression. It acts as a positive allosteric modulator of GABA-A receptors in the brain, aiming to provide rapid relief of depressive symptoms without the side effects associated with traditional antidepressants.

METHODS

Search strategy A systematic literature search was performed in July 1st, 2023, using keywords such as (depress* OR 'affective' OR 'mood') AND ('zuranolone' OR 'SAGE-217' OR 'S-812217') across PubMed, EMBASE, Cochrane CENTRAL, Web of Science, and the ClinicalTrials.gov database. Studies from all languages and regions were included.

Participant or population Participants with a diagnosis of major depressive disorder or postpartum depressionbipolar depression.

Intervention Zuranolone.

Comparator Placebo or different dose of zuranolone.

Study designs to be included RCT.

Eligibility criteria Inclusion criteria comprised (1) randomized controlled trial (RCT) with placebo-controlled; (2) a diagnosis of major depressive disorder or postpartum depressionbipolar depression using diagnostic criteria, such as Diagnostic and Statistical Manual of Mental Disorders; (3) depression severity quantified with eligible scale, both before and after zuranolone regimen. Exclusion criteria consisted of (1) non-randomized trials, such as literature reviews and case reports/series; (2) letters to editors or editorial comments; (3) RCT without placebo controls.

Information sources A systematic literature search was performed in July 1st, 2023, using keywords such as (depress* OR 'affective' OR 'mood') AND ('zuranolone' OR 'SAGE-217' OR 'S-812217') across PubMed, EMBASE, Cochrane CENTRAL, Web of Science, and the ClinicalTrials.gov database.

Main outcome(s) Our primary interest focused on the change in depression score before and after the zuranolone regimen.

Additional outcome(s) Change in anxiety severity, dropout rates, and side effect rates.

Quality assessment / Risk of bias analysis The appraisal for the risk of bias among our included studies was independently performed by two authors, following the risk of bias tool in the Cochrane Handbook.

Strategy of data synthesis We calculated the effect size (ES) to measure the improvement in depressive symptoms resulting from changes in the depression score before and immediately after zuranolone treatment. Additionally, we considered the ES of change in anxiety symptoms and overall improvement as secondary outcome, using the anxiety scale at the same timepoint. As for dichotomous outcomes such as side effect, dropout rate, and depression response/remission rate, were measured with odd ratios (OR). we employed standardized mean difference (SMD) or OR with 95% confidence intervals (95% CIs). In anticipation of potential heterogeneity among various studies, we utilized a random effect model for our meta-analysis.
We also performed a dose-response meta-analysis in a single step method. To assess the relationship between exposure and outcomes, we employed the methods proposed by Greenland and Orsini. These methods allowed us to examine nonlinear trends. To analyze nonlinear dose-response trends, we utilized restricted cubic splines with four knots, namely Placebo, Zuranolone 20mg, Zuranolone 30mg, and Zuranolone 50mg.

Subgroup analysis Major depressive disorder or postpartum depression.

Sensitivity analysis No.

Language restriction No.

Country(ies) involved Taiwan.

Keywords efficacy, safety, zuranolone, major depressive disorder, postpartum depression.

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