INPLASY

Dose-response association of lurasidone in the treatment of bipolar depression: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - National Science and Technology Council (Taiwan): 112-2314-B-182-070-MY3.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202430069

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 March 2024 and was last updated on 16 March 2024.

INTRODUCTION

Review question / Objective PICOS: (1) Patients were diagnosed with a major depressive episode of bipolar disorder; (2) Patients treated with lurasidone; (3) Compared to placebo; (4) Outcomes included changes in depression severity, anxiety severty, overall severity, quality of life, disability, dropout rates, side effect rates, metabolic changes, and endocrine changes after lurasidone treatment; (5) Study design was randomized controlled trial (RCT).

Condition being studied Our study sought to identify RCTs investigating the efficacy and safety of lurasidone for treating bipolar depression. Lurasidone is one of the atypical antipsychotics which is also indicated in bipolar depression. However, lack of evidence had suggested the dosage in bipolar depression. We would like to propose the suggestive dosing based on current evidence in terms of efficacy and safety issue.

METHODS

Participant or population Patients were diagnosed with a major depressive episode of bipolar disorder.

Intervention Lurasidone in different dosage.

Comparator Placebo.

Study designs to be included Randomized controlled trial.

Eligibility criteria The included criteria were: (1) Only randomized controlled trial comparing placebo with lurasidone (with or without coadministration) were eligible. (2) Participants were required to have a diagnosis of bipolar depression based on established criteria. (3) Randomized controlled trials were required to quantify the severity of depression using a validated scale before and after lurasidone administration. The exclusion criteria were: (1) The

study compared lurasidone with other active treatments, without a placebo control group. (2) Study participants had a diagnosis other than bipolar disorder, such as schizophrenia. (3) The study did not report outcomes related to depressive symptoms.

Information sources From database inception to March 1, 2024, encompassing PubMed, EMBASE, Cochrane CENTRAL, Science Direct, and ClinicalTrials.gov.

Main outcome(s) For efficacy assessment, the primary outcome measure of efficacy was change in depression severity after lurasidone treatment. For acceptability assessment, the primary outcome measure was the dropout rate during the study period.

Additional outcome(s) Secondary efficacy outcomes included (1) Change in anxiety severity; (2) Change in overall illness severity; (3) Change in quality of life; (4) Change in disability. Secondary acceptability outcomes included: (1) Any side effects during the study period; (2) Mania or hypomania during the study period; (3) Suicidal ideation and behavior during the study period. Additionally, we were interested in changes in metabolic and endocrine profiles, including (1) Body weight; (2) Lipid profiles; (3) Blood sugar; (4) Prolactin levels.

Quality assessment / Risk of bias analysis Cochrane risk-of-bias tool for randomized trials (RoB 2).

Strategy of data synthesis In the single-step dose-response meta-analysis, we explored the relationship between lurasidone dosage and outcomes. We employed methodologies developed by Greenland and Orsini to account for potential non-linear trends in the data. Specifically, we implemented restricted cubic splines with three knots placed at fixed percentiles (10th, 50th, and 90th) corresponding to different lurasidone doses. All analyses were performed using the dosresmeta package (version 2.0.1) within R software. A two-tailed p-value of less than 0.05 was considered statistically significant.

Subgroup analysis None.

Sensitivity analysis None.

Language restriction No.

Country(ies) involved Taiwan; Australia; Spain.

Keywords Lurasidone; bipolar disorder; depression; BDI; BDII; DRMA.

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