Title of metanalysis :**Vortioxetine for depression in adults: A systematic review and dose-response meta-analysis of randomized controlled trials**

PubMed ID of metaanalysis:38957929

**Search terms**:

| No. | Query | Results |
| --- | --- | --- |
| 1 | depressive disorder[MeSH Terms] OR depressive disorder, major[MeSH Terms] OR mood disorders[MeSH Terms] OR dysthymic disorder[MeSH Terms] OR depression[Text Word] OR depressive[Text Word] OR depressed[Text Word] OR dysthymia[Text Word] OR dysthymic[Text Word] OR affective symptoms[MeSH Terms] OR mdd[Title/Abstract] OR affective disorders[All Fields] | 704661 |
| 2 | "vortioxetine"[MeSH Terms] OR "vortioxetine"[Title/Abstract] OR "Lu AA21004"[All Fields] | 731 |
| 3 | (randomized controlled trial[Publication Type] OR controlled clinical trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR double-blind[Title/Abstract] OR controlled[Title/Abstract] OR randomly[Title/Abstract] OR trial[Title/Abstract] OR groups[Title/Abstract]) NOT ("animals"[MeSH Terms]) | 926749 |
| 4 | 1 AND 2 AND 3 | 66 |

**Inclusion Criteria:**

We included randomized controlled trials meeting the following criteria:

(a) Participant: Adults aged 18 years and older diagnosed withMDD based on versions of the DSM or the SCID (e.g., DSM-IV,SCID-5).

(b) Intervention: Vortioxetine or Lu AA21004.

(c) Comparison: Placebo control or other antidepressants.

(d) Outcome: We included the following outcomes assessed after 6–8 weeks of treatment: (1) Primary outcomes: Change inMontgomery-Åsberg Depression Scale (MADRS)/Hamilton Depres-sion Rating Scale (HAM-D) total score from baseline to the last visit(mean SD) between the intervention and control groups. Any other validated scale was used when these two scales were not available.(2) Secondary outcomes: Response (deﬁned as a reduction of 50% or more in the total score on the scale for depression), dropout for any reason (as an overall measure of treatment acceptability), dropout due to adverse events (as an assessment of tolerability), and the rate of any adverse events (as a safety assessment).

(e) Study design: Only randomized controlled studies were included. For studies examining the dose–response relationship, we included all studies within the same trial comparing two or more ﬁxedor ﬂexible dose treatment groups (including placebo). There were no restrictions on the dose of vortioxetine in the included studies.found in the article text

**Exclusion Criteria:**

We excluded studies meeting any of the following criteria:(1) Patients under 18 or those with other psychiatric disorders(e.g., generalized anxiety disorder, social anxiety disorder, etc.);(2) studies not published in English; (3) studies lacking outcomes of interest to us.

Search Date: 8 February, 2024

Included studies:

| Study title | Pubmed ID of included study |
| --- | --- |
| Alvarez E, Perez V, Dragheim M, Loft H, Artigas F. A double-blind,randomized, placebo-controlled, active reference study of Lu AA21004 inpatients with major depressive disorder. Int. J. Neuropsychopharmacol.2012; 15: 589–600 | * 21767441 |
| Baldwin DS, Loft H, Dragheim M. A randomised, double-blind, placebo controlled, duloxetine-referenced, ﬁxed-dose study of three dosages of Lu AA21004 in acute treatment of major depressive disorder (MDD).Eur. Neuropsychopharmacol. 2012; 22: 482–491 | * 22209361 |
| Henigsberg N, Mahableshwarkar AR, Jacobsen P, Chen Y, Thase ME. A randomized, double-blind, placebo-controlled 8-week trial of the efﬁcacyand tolerability of multiple doses of Lu AA21004 in adults with major depressive disorder. J. Clin. Psychiatry 2012; 73: 953–959. | * 22901346 |
| Katona C, Hansen T, Olsen CK. A randomized, double-blind, placebo-controlled, duloxetine-referenced, ﬁxed-dose study comparing theefﬁcacy and safety of Lu AA21004 in elderly patients with major depres-sive disorder. Int. Clin. Psychopharmacol. 2012; 27: 215–223 | * 22572889 |
| Jain R, Mahableshwarkar AR, Jacobsen PL, Chen Y, Thase ME. A ran-domized, double-blind, placebo-controlled 6-wk trial of the efﬁcacy and tolerability of 5 mg vortioxetine in adults with major depressive disorder.Int. J. Neuropsychopharmacol. 2013; 16: 313–321. | * 22963932 |
| Mahableshwarkar AR, Jacobsen PL, Chen Y. A randomized, double-blind trial of 2.5 mg and 5 mg vortioxetine (Lu AA21004) versus placebo for 8 weeks in adults with major depressive disorder. Curr. Med.Res. Opin. 2013; 29: 217–226. | * 23252878 |
| Boulenger JP, Loft H, Olsen CK. Efﬁcacy and safety of vortioxetine(Lu AA21004), 15 and 20 mg/day: A randomized, double-blind,placebo-controlled, duloxetine-referenced study in the acute treatment of adult patients with major depressive disorder. Int. Clin.Psychopharmacol. 2014; 29: 138–149 | * 24257717 |
| McIntyre RS, Lophaven S, Olsen CK. A randomized, double-blind,placebo-controlled study of vortioxetine on cognitive function in depressed adults. Int. J. Neuropsychopharmacol. 2014; 17: 1557–1567. | * 24787143 |
| Montgomery SA, Nielsen RZ, Poulsen LH, Haggstrom L. A randomised,double-blind study in adults with major depressive disorder with an inadequate response to a single course of selective serotonin reuptake inhibitor or serotonin-noradrenaline reuptake inhibitor treatment switched to vortioxetine or agomelatine. Hum. Psychopharmacol. 2014; 29:470–482 | * 25087600 |
| Jacobsen PL, Mahableshwarkar AR, Serenko M, Chan S, Trivedi MH. A randomized, double-blind, placebo-controlled study of the efﬁcacy andsafety of vortioxetine 10 mg and 20 mg in adults with major depressive disorder. J. Clin. Psychiatry 2015; 76: 575–582 | * 26035185 |
| Mahableshwarkar AR, Jacobsen PL, Chen Y, Serenko M, Trivedi MH.A randomized, double-blind, duloxetine-referenced study comparing efﬁ-cacy and tolerability of 2 ﬁxed doses of vortioxetine in the acute treat-ment of adults with MDD. Psychopharmacology 2015; 232: 2061–2070 | * 25575488 |
| Mahableshwarkar AR, Jacobsen PL, Serenko M, Chen Y, Trivedi MH.A randomized, double-blind, placebo-controlled study of the efﬁcacy andsafety of 2 doses of vortioxetine in adults with major depressive disorder.J. Clin. Psychiatry 2015; 76: 583–591. | * 26035186 |
| Mahableshwarkar AR, Zajecka J, Jacobson W, Chen Y, Keefe RS. A randomized, placebo-controlled, active-reference, double-blind, ﬂexible-dose study of the efﬁcacy of vortioxetine on cognitive function in major depressive disorder. Neuropsychopharmacology 2015; 40: 2025–2037 | * 25687662 |
| Wang G, Gislum M, Filippov G, Montgomery S. Comparison of vortioxetine versus venlafaxine XR in adults in Asia with major depres-sive disorder: A randomized, double-blind study. Curr. Med. Res. Opin.2015; 31: 785–794 | * 25650503 |
| Baune BT, Sluth LB, Olsen CK. The effects of vortioxetine on cognitive performance in working patients with major depressive disorder: A short-term, randomized, double-blind, exploratory study. J. Affect. Dis-ord. 2018; 229: 421–428. | * 29331703 |
| Inoue T, Nishimura A, Sasai K, Kitagawa T. Randomized, 8-week,double-blind, placebo-controlled trial of vortioxetine in Japanese adults with major depressive disorder, followed by a 52-week open-label exten-sion trial. Psychiatry Clin. Neurosci. 2018; 72: 103–115 | * 29160598 |
| Nishimura A, Aritomi Y, Sasai K, Kitagawa T, Mahableshwarkar AR.Randomized, double-blind, placebo-controlled 8-week trial of the efﬁ-cacy, safety, and tolerability of 5, 10, and 20 mg/day vortioxetine in adults with major depressive disorder. Psychiatry Clin. Neurosci. 2018;72: 64–72. | * 28858412 |
| Vieta E, Sluth LB, Olsen CK. The effects of vortioxetine on cognitive dys-function in patients with inadequate response to current antidepressants in major depressive disorder: A short-term, randomized, double-blind, explor-atory study versus escitalopram. J. Affect. Disord. 2018; 227: 803–809. | * 29673132 |
| Borhannejad F, Shariati B, Naderi S et al. Comparison of vortioxetine and sertraline for treatment of major depressive disorder in elderly patients: Adouble-blind randomized trial. J. Clin. Pharm. Ther. 2020; 45: 804–811. | * 32420649 |
| Inoue T, Sasai K, Kitagawa T, Nishimura A, Inada I. Randomized,double-blind, placebo-controlled study to assess the efﬁcacy and safety of vortioxetine in Japanese patients with major depressive disorder.Psychiatry Clin. Neurosci. 2020; 74: 140–148. | * 31725942 |
| Lee SH, Jeon SW, Shin C et al. Acute efﬁcacy and safety of escitalopram versus desvenlafaxine and vortioxetine in the treatment of depression with cognitive complaint: A rater-blinded randomized com-parative study. Psychiatry Investig. 2022; 19: 500 | * 35753689 |
| McIntyre RS, Florea I, Pedersen MM, Christensen MC. Head-to-head comparison of vortioxetine versus desvenlafaxine in patients with major depressive disorder with partial response to SSRI therapy. J. Clin. Psychi-atry 2023; 84: 23m14780. | * 37227402 |
| Shin C, Jeon SW, Lee S-H et al. Efﬁcacy and safety of escitalopram,desvenlafaxine, and vortioxetine in the acute treatment of anxious depression: A randomized rater-blinded 6-week clinical trial. Clin.Psychopharmacol. Neurosci. 2023; 21: 135–146. | * 36700320 |