Conclusions: Treatment-resistant patients in a major depressive episode showed a rapid antidepressant response to a single infusion of ketamine. The current study represents the largest investigation to date of ketamine in TRD. Utilizing an optimized active placebo design, the trial provides new evidence for the specific antidepressant effects of ketamine, apart from its non-specific anesthetic properties. Future research is required to test the antidepressant effects of ketamine beyond a single administration and to characterize its longer-term safety profile.

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P.2.f.029 A randomised, double-blind, study of vortioxetine versus agomelatine in adults with major depressive disorder (MDD) with inadequate response to SSRI/SNRI treatment

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Objective: Data from randomized trials comparing treatment strategies in patients who were unresponsive to first-line antidepressant treatment are limited. Vortioxetine (Lu AA21004) is an investigational multimodal antidepressant thought to work through a combination of 2 pharmacological modes of action: serotonin (5-HT) receptor activity modulation and 5-HT reuptake inhibition [1,2]. This multi-national study compared the efficacy and tolerability of flexible-dose treatment with vortioxetine (10–20 mg/day) versus agomelatine (25–50 mg/day) in adult patients with major depressive disorder (MDD) who presented with an inadequate response to SSRI/SNRI monotherapy (citalopram, escitalopram, paroxetine, sertraline, duloxetine, venlafaxine), wanted to switch treatment and were, in the investigator's clinical opinion, candidates for a treatment switch from their current treatment.

Methods: This was a double-blind, randomized, 12-week comparator study. The primary efficacy endpoint was the change from baseline to Week 8 in Montgomery–Åsberg Depression Rating Scale (MADRS) total score in the full-analysis set (FAS) analysed by mixed model repeated measures (MMRM) using a non-inferiority test. Pre-defined secondary efficacy endpoints included clinician-rated assessment of remission (MADRS total score $\leqslant$10), anxiety symptoms (Hamilton Anxiety Rating Scale [HAM-A]), global clinical judgment using the Clinical Global Impression scales for severity (CGI-S) and improvement (CGI-I). It also included patient-reported outcomes assessing overall functioning (Sheehan Disability Scale [SDS]), health-related quality of life (HRQoL, EuroQol [EQ-5D]), productivity (Work Limitation Questionnaire [WLQ]), and family functioning (Depression and Family Functioning Scale [DFFS]).

Results: Eligible patients were randomized (1:1) to vortioxetine (10–20 mg/day) or agomelatine (25–50 mg/day) for 12 weeks of double-blind treatment. On the primary efficacy endpoint, vortioxetine (n = 252) was statistically significantly superior to agomelatine (n = 241) ($p < 0.05$) by 2.2 MADRS points. Significant differences in favour of vortioxetine were found for the MADRS, HAM-A, CGI-S and CGI-I from Week 4 onwards (FAS, MMRM; $p < 0.05$) and robustness was confirmed by significant differences by ANCOVA (FAS, LOCF). Remission rates for vortioxetine versus agomelatine (LOCF) were 40.5% versus 29.5% ($p = 0.0054$) at Week 8 and 55.2% versus 39.4% ($p = 0.0002$) at Week 12. For patient-reported outcomes relating to functioning and HRQoL, significant differences in favour of vortioxetine were found for the SDS and the EQ-5D from Week 4 onwards, for the DFFS at Weeks 8 and 12 and for the WLQ at Week 8 (FAS, MMRM; $p < 0.05$).

Robustness was confirmed by significant differences using ANCOVA (FAS, LOCF). Fewer patients withdrew due to adverse events with vortioxetine (5.9%) than agomelatine (9.5%). Adverse events with an incidence $\geqslant$5% with either treatment were nausea (16.2% vs 9.1%), headache (10.3% vs 13.2%), dizziness (7.1% vs 11.6%) and somnolence (4.0% vs 7.9%) for vortioxetine and agomelatine, respectively.

Conclusions: The primary efficacy endpoint of this comparator study was met, with vortioxetine also showing a significant benefit compared to agomelatine in difficult to treat MDD patients who directly switched antidepressant treatment after an inadequate response to SSRI/SNRI treatment. Statistically significant differences in favour of vortioxetine were seen for secondary efficacy outcomes including patient-reported outcomes that evaluated overall functioning and HRQoL. This study confirms that vortioxetine is efficacious and well-tolerated

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P.2.f.030 Are there differences in treatment of acute manic episodes in bipolar patients with or without comorbid borderline personality disorder?

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Purpose of the study: To compare epidemiological, clinical and pharmacological endpoints in bipolar disorder patients (BD) hospitalized because manic episode with or without comorbid borderline personality disorder (BPD).