

# Real-world effectiveness of esketamine nasal spray in treatment resistant depression: results from the ECHO prospective non-interventional cohort study

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## Introduction

- Esketamine nasal spray (NS), in combination with a selective serotonin reuptake inhibitor (SSRI)/serotonin-norepinephrine reuptake inhibitor (SNRI), is approved for patients with treatment resistant depression (TRD).<sup>1</sup>
- Existing short- and long-term clinical data for esketamine NS indicate that patients achieve rapid and persistent reductions in depressive symptoms.<sup>2,3</sup>
- Given treatment goals extend beyond symptom reduction to sustained response and remission, and relapse prevention, evaluating long-term effectiveness in real-world populations remains a key consideration.
- Here, we evaluate the long-term effectiveness of esketamine NS, in combination with antidepressants, for the treatment of adults with TRD in real-world clinical settings using data from the Esketamine CoHort (ECHO) study.

## Methods

- ECHO was a long-term, prospective, non-interventional study conducted in seven countries (Belgium, Germany, Israel, Italy, Netherlands, Spain and Sweden).
- Eligible patients were adults diagnosed with TRD prescribed esketamine NS per local clinical practice, independent of study participation.
- The study included a variable-length esketamine NS treatment period and a 6-month post-treatment follow-up period.
- Clinical outcomes reported include the proportion of patients with overall responses (≥50% improvement in Montgomery-Åsberg Depression Rating Scale [MADRS] from treatment initiation), clinically meaningful and clinically substantial improvements (≥6- and 12-point reduction in MADRS score), remission (MADRS ≤10), and relapse (after achieving remission/response during the treatment period), and MADRS total scores.
- Data are reported for the full analysis set up to 48 weeks of the treatment period.

## Results

- Overall, 570 patients were enrolled in the treatment period; baseline characteristics have been reported previously and were representative of severe and chronic TRD.<sup>4</sup>
- Overall response (≥50% reduction in MADRS total score) rates were improved during the treatment period, from 8.0% (35/436) at Week 2 to 57.0% (81/142) at Week 48 (**Figure 1**).
  - The proportion of patients who achieved clinically meaningful and clinically substantial improvements (≥6- and 12-point reduction in MADRS score) increased from 49.1% (214/436)/22.5% (98/436) at Week 2 to 85.9% (122/142)/70.4% (100/142) at 48 weeks of treatment, respectively (**Figure 2**).
- Remission (MADRS total score ≤10) rates also increased during the 48-week treatment period, from 3.4% (15/436) at Week 2 to 33.8% (48/142) at Week 48 (**Figure 3**).
- Patients with a ≤2-year duration of major depressive episode had higher overall response and remission rates than those with >2-year duration (**Figures 1 and 3**).
- Among the 302 patients achieving response/remission during the treatment period, 71 (23.5%) experienced a relapse, most commonly defined according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (62.0% [44/71]; **Table 1**).<sup>5</sup>
- Mean (SD) MADRS total scores improved from baseline (33.3 [6.8]) to Week 2 (26.7 [8.2]), and throughout the treatment period to Week 48 (15.5 [10.0]).
  - Results for MADRS total scores were similar regardless of the number of previous treatment failures.

### Strengths and limitations

- Data from ECHO represent the largest real-world dataset for esketamine NS, and reflect the complexity of the real-world population of patients with TRD, although limitations include a lack of comparator arm.

Figure 1. Response rates during esketamine NS treatment, overall and by duration of current major depressive episode

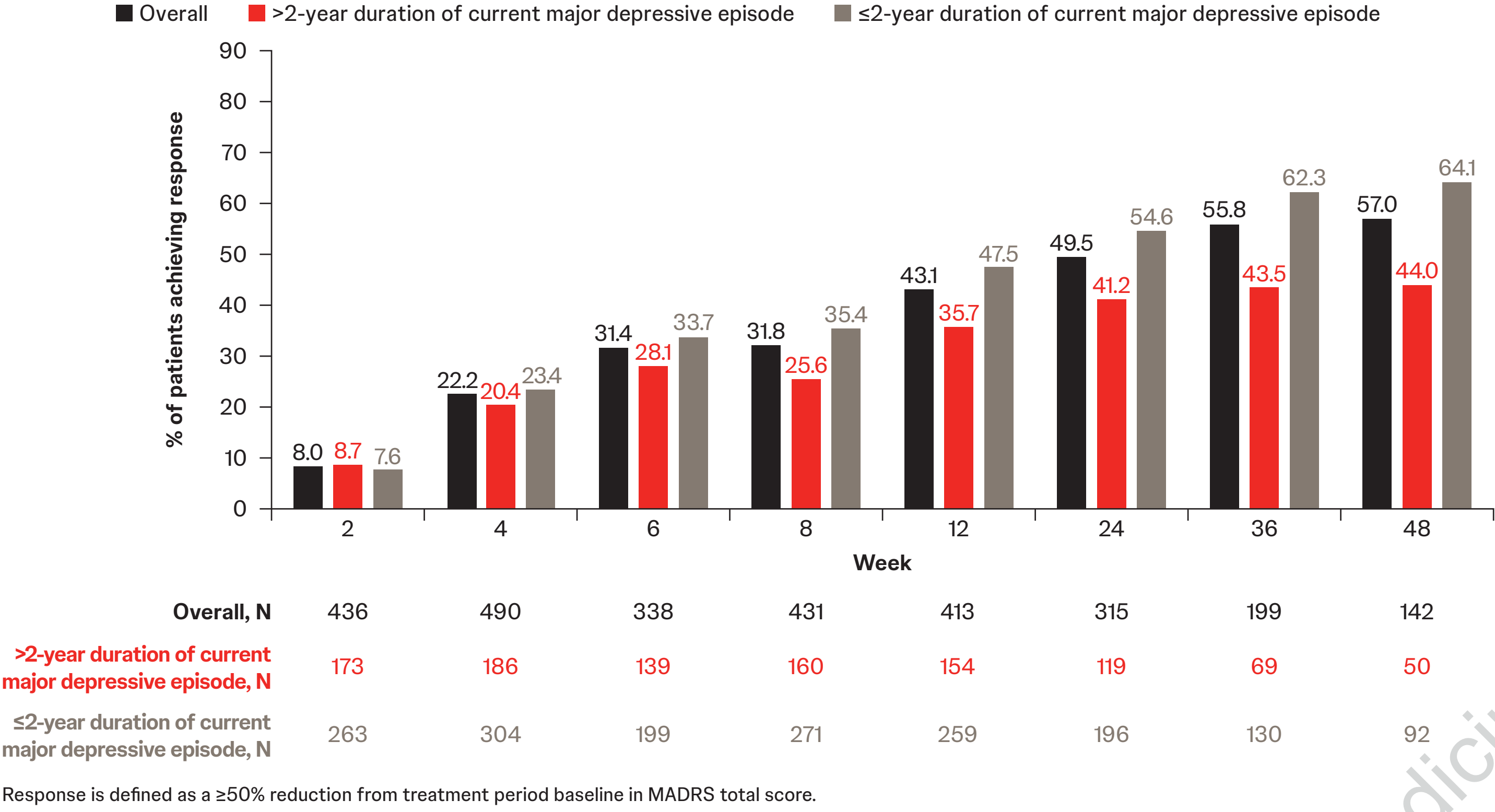


Figure 2. Rates of clinically meaningful and clinically substantial improvements in MADRS total score during esketamine NS treatment

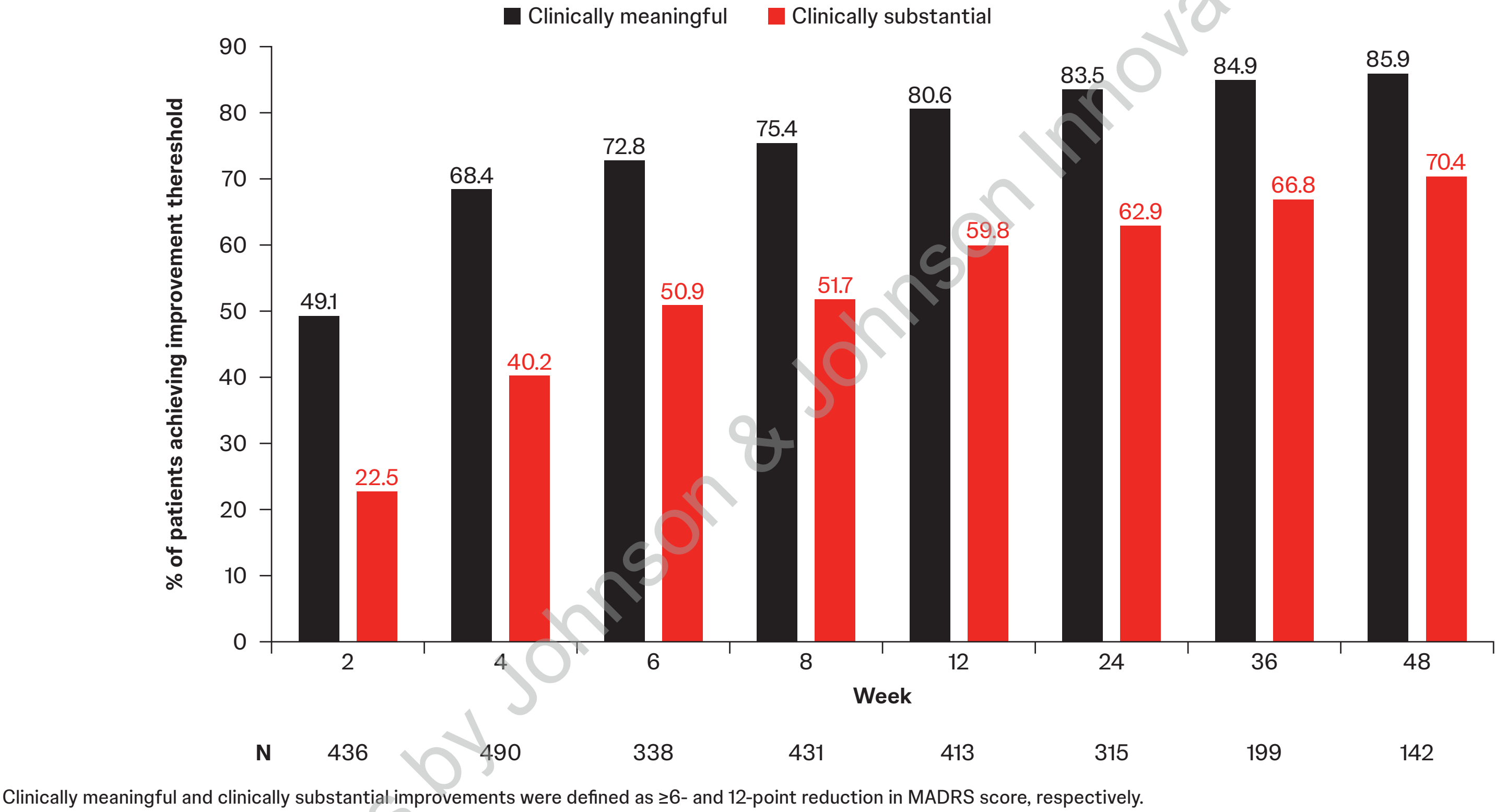


Figure 3. Remission rates during esketamine NS treatment, overall and by duration of current major depressive episode

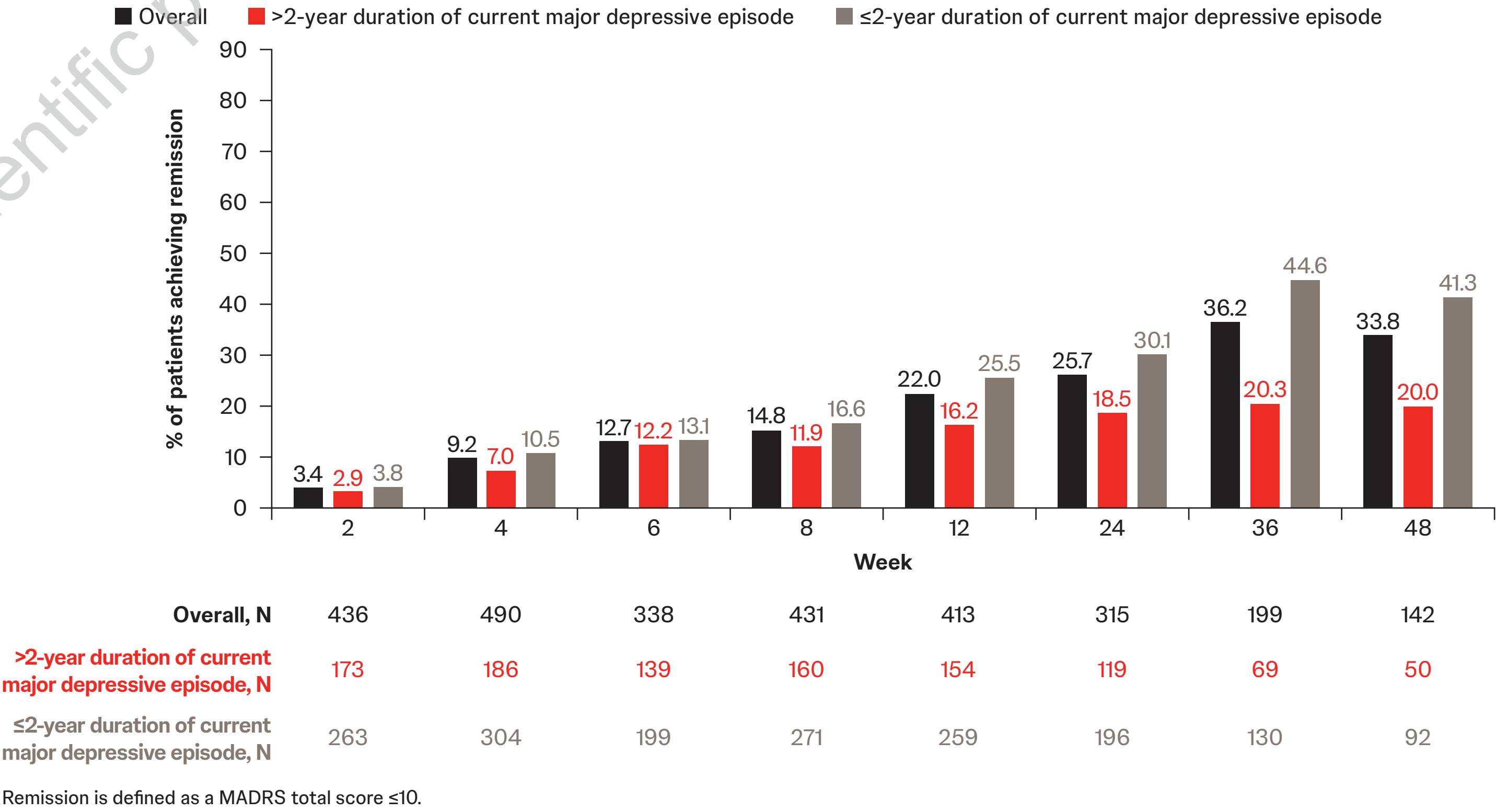


Table 1. Patients experiencing relapses

| n/N (%), unless otherwise specified                                                                    | Total          |
|--------------------------------------------------------------------------------------------------------|----------------|
| Proportion of patients who achieved response or remission at any timepoint during the treatment period | 302/570 (53.0) |
| Proportion of patients with relapse                                                                    | 71/302 (23.5)  |
| Time to first relapse, days, mean (SD)                                                                 | 161.2 (213.1)  |
| Definition of first relapse                                                                            |                |
| Defined according to DSM-5 criteria                                                                    | 44/71 (62.0)   |
| MADRS total score ≥22                                                                                  | 24/71 (33.8)   |
| Suicide attempt                                                                                        | 2/71 (2.8)     |
| Hospitalisation                                                                                        | 1/71 (1.4)     |

## Key takeaway



- Increasing response and remission rates over time, combined with low relapse rates, in this real-world patient population reinforce the short- and long-term effectiveness of esketamine NS observed in previous clinical trials, supporting it as a valuable therapeutic strategy for patients with TRD.

## Conclusions



- Esketamine NS resulted in clinically meaningful and sustained improvements in depressive symptoms, with increasing response and remission rates over time.
- These data support the effectiveness of esketamine NS across patients with shorter and longer current episodes.
  - Higher response and remission rates in patients with shorter episodes indicate that earlier initiation of esketamine NS treatment is associated with improved clinical outcomes.
- Relapse rates during the treatment period were low among patients who had achieved response/remission, and time to first relapse appeared relatively extended compared with previous reports, supporting the durability of treatment benefit with esketamine NS.<sup>6</sup>

## Abbreviations

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ECHO: Esketamine CoHort; MADRS: Montgomery-Åsberg Depression Rating Scale; NS: nasal spray; SD: standard deviation; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; TRD: treatment resistant depression.

## Author contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: SK, YG, LH, AI, VM, CR-L, JR, GR, IT, BTB; drafting of the publication, or reviewing it critically for important intellectual content: SK, YG, LH, AI, VM, CR-L, JR, GR, IT, BTB; final approval of the publication: SK, YG, LH, AI, VM, CR-L, JR, GR, IT, BTB.

## Disclosures

SK: Participated in advisory boards and received speaker's honoraria over the last 3 years from ARISTO Pharma, Johnson & Johnson, Medice and Otsuka; participated in clinical studies in esketamine NS. YG, IT, JR: Employees of Johnson & Johnson; hold Johnson & Johnson company stock/stock options. LH: Participated in advisory boards and received speaker's honoraria over the last 3 years from Johnson & Johnson and Lundbeck; participated in clinical studies on esketamine NS. AI: Received research or travel support from or served as speaker or advisor for Alter, Casen Recordati, Janssen-Cilag, Lundbeck, Otsuka Pharmaceutical SA, Rovi and Viatrix. VM: Served on advisory boards, received consulting fees and speaker's honoraria from Johnson & Johnson (Europe and Italy), Lundbeck, Otsuka, Teva Italia and Teva Europe; received travel grants from Angelini, Johnson & Johnson, Lundbeck, Otsuka and Teva. CR-L: Participated in advisory boards and received speaker's honoraria from CAMPUS, Johnson & Johnson, LivaNova and Medice. GR: Speaker/consultant for Angelini, Johnson & Johnson, Lundbeck, Neuraxpharm, Otsuka and Rovi. BTB: Received consulting fees for roles with the National Health and Medical Research Council, Australia; received honoraria from Angelini, AstraZeneca, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, GH Research, Johnson & Johnson, LivaNova, Lundbeck, Medscape, Otsuka, Pfizer, Roche, Servier, Sumitomo Dainippon Pharma, Sunovion, Viatrix and Wyeth; served on advisory boards for Biogen, Boehringer Ingelheim, GH Research, Janssen-Cilag, LivaNova, Lundbeck, Medscape, Novartis, Viatrix and Otsuka; received research grants from private industries or non-profit funds from AstraZeneca, Janssen, Lundbeck and Sanofi-Synthelabo; received research grants from the BMBF and BMG Germany, the DFG, Germany, the National Health and Medical Research Council (NHMRC, Australia), Medical Research Future Fund (MRFF, Australia), Horizon Europe 2021, EraPerMed and the Wellcome Trust (UK); received research grants from the Fay Fuller Foundation and James & Diana Ramsay Foundation, Adelaide.

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