**Supplemental Table 1.** Mean scores of the rating scales measuring efficacy and safety outcomes between responders and nonresponders at t+24h after the sixth infusion.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Primary and secondary outcomes | | Total sample  (n=77) | | Nonresponders  (n=25) | | Responders  (n=52) | | Statistics | |
| Mean | SD | Mean | SD | Mean | SD | *p* | Cohen’s *d*c |
| 4 h | MADRS score | 25.6 | 8.9 | 28.9 | 8.7 | 24.0 | 8.6 | **0.03** | 0.57 |
| SSI-5 termsa | 1.5 | 2.5 | 1.7 | 2.2 | 1.4 | 2.7 | 0.44 | 0.12 |
| HAMA score | 15.0 | 7.0 | 18.0 | 7.6 | 13.6 | 6.2 | **0.01** | 0.63 |
| CADSS score | 0.8 | 2.3 | 1.0 | 2.5 | 0.7 | 2.2 | 0.37 | 0.13 |
| BPRS-4 itemsb | 4.2 | 0.7 | 4.1 | 0.4 | 4.2 | 0.8 | 0.18 | -0.16 |
| 24 h | MADRS score | 25.6 | 10.3 | 28.7 | 9.6 | 24.1 | 10.4 | **0.04** | 0.46 |
| SSI-5 termsa | 1.3 | 2.3 | 1.8 | 2.4 | 1.1 | 2.3 | 0.12 | 0.30 |
| HAMA score | 16.0 | 7.7 | 18.3 | 7.6 | 14.8 | 7.6 | **0.04** | 0.46 |
| CADSS score | 0.3 | 1.3 | 0.2 | 0.6 | 0.4 | 1.5 | 0.38 | -0.18 |
| BPRS-4 itemsb | 4.1 | 0.5 | 4.1 | 0.4 | 4.1 | 0.5 | 0.97 | 0 |
| 3 days | MADRS | 23.0 | 10.3 | 27.5 | 9.6 | 20.9 | 10.0 | **0.004** | 0.67 |
| SSI-5 termsa | 0.9 | 1.8 | 1.1 | 1.6 | 0.8 | 1.9 | 0.39 | 0.17 |
| HAMA score | 13.9 | 7.4 | 16.8 | 8.4 | 12.5 | 6.6 | **0.01** | 0.57 |
| CADSS score | 0.4 | 1.2 | 0.2 | 0.6 | 0.4 | 1.4 | 0.42 | -0.19 |
| BPRS-4 itemsb | 4.1 | 0.4 | 4.1 | 0.3 | 4.1 | 0.5 | 0.89 | 0 |
| 4 days | MADRS | 22.7 | 9.9 | 28.6 | 8.9 | 19.9 | 9.2 | **<0.001** | 0.96 |
| SSI-5 termsa | 1.1 | 1.9 | 1.4 | 1.9 | 0.9 | 2.0 | 0.34 | 0.26 |
| HAMA score | 14.2 | 7.5 | 18.3 | 8.6 | 12.2 | 6.1 | **0.001** | 0.82 |
| CADSS score | 0.1 | 0.7 | 0.2 | 0.6 | 0.1 | 0.7 | 0.71 | 0.15 |
| BPRS-4 itemsb | 4.1 | 0.3 | 4.1 | 0.4 | 4.0 | 0.1 | 0.38 | 0 |
| 5 days | MADRS | 21.4 | 10.4 | 27.9 | 9.9 | 18.3 | 9.2 | **<0.001** | 1.00 |
| SSI-5 termsa | 0.8 | 1.6 | 1.5 | 2.0 | 0.5 | 1.2 | **0.02** | 0.61 |
| HAMA score | 12.5 | 6.9 | 16.4 | 8.0 | 10.7 | 5.4 | **0.001** | 0.84 |
| CADSS score | 0.2 | 1.3 | 0.7 | 2.2 | 0 | 0 | **0.01** | 0.45 |
| BPRS-4 itemsb | 4.0 | 0.2 | 4.0 | 0.2 | 4.0 | 0.1 | 0.85 | 0 |
| 6 days | MADRS | 19.8 | 10.4 | 25.9 | 9.9 | 16.8 | 9.3 | **<0.001** | 0.95 |
| SSI-5 termsa | 0.7 | 1.3 | 1.2 | 1.7 | 0.4 | 1.0 | 0.08 | 0.57 |
| HAMA score | 12.1 | 6.8 | 15.4 | 8.2 | 10.5 | 5.4 | **0.006** | 0.71 |
| CADSS score | 0.01 | 0.2 | 0.1 | 0.3 | 0.02 | 0.1 | 0.83 | 0.36 |
| BPRS-4 itemsb | 4.1 | 0.4 | 4.1 | 0.6 | 4.1 | 0.2 | 0.58 | 0 |
| 8 days | MADRS | 18.4 | 10.0 | 24.9 | 10.6 | 15.3 | 8.1 | **<0.001** | 1.02 |
| SSI-5 termsa | 0.6 | 1.3 | 1.2 | 1.8 | 0.3 | 0.8 | **0.04** | 0.65 |
| HAMA score | 11.3 | 7.0 | 14.9 | 8.5 | 9.6 | 5.5 | **<0.001** | 0.74 |
| CADSS score | 0.2 | 0.9 | 0.1 | 0.4 | 0.2 | 1.1 | 0.63 | -0.12 |
| BPRS-4 itemsb | 4.0 | 0.3 | 4.1 | 0.4 | 4.0 | 0.1 | 0.59 | 0.34 |
| 9 days | MADRS | 17.7 | 10.9 | 26.5 | 11.0 | 13.5 | 8.1 | **<0.001** | 1.35 |
| SSI-5 termsa | 0.5 | 1.2 | 1.2 | 1.8 | 0.2 | 0.6 | **0.02** | 0.75 |
| HAMA score | 11.0 | 7.3 | 16.2 | 8.8 | 8.5 | 4.8 | **<0.001** | 1.09 |
| CADSS score | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| BPRS-4 itemsb | 4.1 | 0.4 | 4.1 | 0.6 | 4.0 | 0.1 | 0.38 | 0.23 |
| 10 days | MADRS | 17.0 | 11.1 | 25.6 | 11.2 | 12.9 | 8.5 | **<0.001** | 1.28 |
| SSI-5 termsa | 0.5 | 1.3 | 1.2 | 1.8 | 0.2 | 0.8 | **0.03** | 0.72 |
| HAMA score | 10.6 | 7.5 | 15.5 | 8.2 | 8.3 | 5.8 | **<0.001** | 1.01 |
| CADSS score | 0.01 | 0.1 | 0.04 | 0.2 | 0 | 0 | 0.89 | 0.28 |
| BPRS-4 itemsb | 4.0 | 0.3 | 4.1 | 0.6 | 4.0 | 0 | 0.29 | 0.24 |
| 11 days | MADRS | 16.6 | 11.5 | 26.6 | 10.9 | 11.8 | 8.2 | **<0.001** | 1.53 |
| SSI-5 termsa | 0.6 | 1.4 | 1.2 | 2.0 | 0.3 | 0.8 | **0.02** | 0.59 |
| HAMA score | 10.6 | 7.6 | 16.2 | 8.5 | 8.0 | 5.4 | **<0.001** | 1.15 |
| CADSS score | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| BPRS-4 itemsb | 4.1 | 0.4 | 4.1 | 0.4 | 4.1 | 0.4 | 0.58 | 0 |
| 12 days | MADRS | 16.3 | 12.7 | 27.8 | 11.1 | 10.8 | 9.3 | **<0.001** | 1.66 |
| SSI-5 termsa | 0.5 | 1.3 | 1.2 | 1.8 | 0.3 | 0.9 | **0.04** | 0.63 |
| HAMA score | 10.4 | 8.2 | 17.0 | 8.9 | 7.2 | 5.6 | **<0.001** | 1.32 |
| CADSS score | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| BPRS-4 itemsb | 4.0 | 0.3 | 4.1 | 0.4 | 4.0 | 0 | 0.29 | 0.35 |
| 13 days | MADRS | 13.5 | 10.1 | 24.6 | 9.5 | 8.1 | 4.5 | **<0.001** | 2.22 |
| SSI-5 termsa | 0.5 | 1.3 | 1.2 | 1.8 | 0.3 | 0.9 | **0.04** | 0.63 |
| HAMA score | 15.4 | 10.7 | 22.9 | 9.3 | 11.8 | 9.4 | **<0.001** | 1.19 |
| CADSS score | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| BPRS-4 itemsb | 4.0 | 0.3 | 4.1 | 0.4 | 4.0 | 0 | 0.29 | 0.35 |
| 26 days | MADRS | 16.9 | 13.4 | 27.3 | 10.8 | 11.9 | 11.5 | **<0.001** | 1.38 |
| SSI-5 termsa | 0.9 | 2.0 | 1.4 | 1.9 | 0.7 | 2.0 | 0.15 | 0.36 |
| HAMA score | 12.0 | 9.5 | 17.8 | 9.8 | 9.1 | 8.0 | **<0.001** | 0.97 |
| CADSS score | 0.1 | 0.5 | 0.04 | 0.2 | 0.1 | 0.6 | 0.89 | -0.13 |
| BPRS-4 itemsb | 4.1 | 0.5 | 4.2 | 0.8 | 4.0 | 0.1 | 0.19 | 0.35 |
| aWe scored the sum of the five items in Part 1.  bIncluding suspiciousness, unusual thought content, hallucinations, and conceptual disorganization.  cPositive effect sizes indicate lower values for responders, and negative effect sizes indicate lower values for nonresponders.  Bolded values are p<0.05.  Abbreviations: -=not applicable; BPRS=the Brief Psychiatric Rating Scale; CADSS=the Clinician Administered Dissociative States Scale; HAMD-17=the 17-item Hamilton Rating Scale for Depression; HAMA=the Hamilton Anxiety Scale; MADRS=the Montgomery-Asberg Depression Rating Scale; SSI=Scale for Suicidal Ideations. | | | | | | | | | |

**Supplemental Figure 1.** Mean SSI-five terms total score following repeated ketamine infusions in patients with major depressive disorder.



\*Mean SSI-5 terms total score is significantly decreased at a given assessment time point compared to baseline (p<0.05).

#Mean SSI-5 terms total score is significantly different at a given assessment time point between responder and nonresponder subgroups at t+24h after the sixth infusion (p<0.05).

Abbreviations: SSI=Scale for Suicidal Ideations; SE=standard error.

**Supplemental Figure 2.** Mean HAMA total score following repeated ketamine infusions in patients with major depressive disorder.



\*Mean HAMA total score is significantly decreased at a given assessment time point compared to baseline (p<0.05).

#Mean HAMA total score is significantly different at a given assessment time point between responder and nonresponder subgroups at t24h after the sixth infusion (p<0.05).

Abbreviations: HAMA=Hamilton Anxiety Scale; SE=standard error.

**Supplemental Figure 3.** Mean BPRS-4 items total score following repeated ketamine infusions in patients with major depressive disorder.



\*Mean BPRS-4 items total score is significantly decreased at a given assessment time point compared to baseline (p<0.05).

#Mean BPRS-4 items total score is significantly different at a given assessment time point between responder and nonresponder subgroups at t+24h after the sixth infusion (p<0.05).

Abbreviations: BPRS=the Brief Psychiatric Rating Scale; SE=standard error.

**Supplemental Figure 4.** Mean CADSS total score following repeated ketamine infusions in patients with major depressive disorder.



\*Mean CADSS total score is significantly decreased at a given assessment time point compared to baseline (p<0.05).

#Mean CADSS total score is significantly different at a given assessment time point between responder and nonresponder subgroups at t+24h after the sixth infusion (p<0.05).

Abbreviations: CADSS=the Clinician Administered Dissociative States Scale; SE=standard error.