List of Institutional Review Boards and Independent Ethics Committees

ARGENTINA*
- Comité de Ética e Investigación del Sanatorio, Cordoba
- Comite de Ética del Instituto Medico Platense CEDIMP, Buenos Aires
- Comité de Ética en Investigación Clínica Privada de Salud Mental Stanta Teresa de Avila, Buenos Aires
- Comité de Ética de CER Investigaciones Clínicas – CECIC, Buenos Aires
- Comité de Ética en Investigacion Burzaco Comité de Etica en Investigacion Burzaco, Buenos Aires
- Comité de Ética en Investigaciones FLENI, Buenos Aires

AUSTRIA
- Ethikkkommission der Med. Universität Wien, und des Allgemeinen Krhs. der Stadt Wien, Wein
- Kepler Universitätsklinikum Ethikkommission des Landes Oberösterreich, Linz

BELGIUM*
- Ethisch Comité g UZ Gent, Gent
- O.L.V. Ziekenhuis IRB, Aalst
- Toetsingscommissie Ethiek GGZ Broeders van liefde, Bierbeek

BRAZIL*
- National Committee of Ethics in Research (CONEP), Brasilia
- Comite de Etica em Pesquisa da UFMG – COEP, Belo Horizonte
- Comitê de Ética em Pesquisa do Investiga - Instituto De Pesquisas, Campinas
- Comitê de Ética em Pesquisa da Faculdade de Medicina do ABC, Santo Andre
- Comite de Ética em Pesquisa do Hospital Universitário, Salvador & Fortaleza
- Comitê de Ética em Pesquisa do Hospital São Carlos, Fortaleza, Ceará
- Comissao de Etica para analise de projetos de pequisa - CAPPesq-HCFMUSP, San Paulo

CANADA
- St. Michael's Hospital Research Ethics Board, Toronto, Ontario

CZECH REPUBLIC*
- Eticka komise Ustredni vojenske nemocnice Praha, Prague
- Eticka komise IKEM a Thomayerovy nemocnice, Prague
- Fakultni nemocnice Brno IRB-EC, Brno

FRANCE
- CPP Sud-Ouest et Outre-Mer III, Service de Pharmacologie Clinique, Leon

LITHUANIA
- Lithuanian Bioethics Committee, Vilnius

POLAND

Niezalezna Komisja Bioetyczna do Spraw Badan Naukowych przy Gdanskim Uniwersytecie Medycznym, Gdansk

SPAIN

Hospital de Navarra - Ceic de Navarra, Pamplona

TURKEY

Uludag University Medical Faculty Clinical Research Ethics Committee, Bursa

UNITED STATES

Biomedical Research Alliance of New York IRB (Lake Success, NY)
Chesapeake IRB (Columbia, MD)
John Hopkins Medicine IRB (Baltimore, MD)
Sharp HealthCare Institutional Review Board (San Diego, CA)
Springfield Committee for Research Involving Human Subjects (SCRIHS) (Springfield, IL)
Sterling Institutional Review Board (Atlanta, GA)
UCSD Human Subjects Research Protection Program (La Jolla, CA)
University of Conneticut School of Medicine IRB (Farmington, CT)
University of North Carolina at Chapel Hill - Office of Research Ethics, Chapel Hill, NC
Western Institutional Review Board (Puyallup, WA)

* Two or more Independent Ethics Committees approved the study protocol/amendments at sites in Argentina, Belgium, Brazil, and Czech Republic.

Patient Inclusion and Exclusion Criteria

Screening for eligible subjects should be performed within 48 hours prior to the first administration of intranasal study drug (if possible, screening should occur within 24 hours prior to the first administration of intranasal study drug).

The inclusion and exclusion criteria for enrolling subjects in this study are described in the following 2 subsections. If there is a question about the inclusion or exclusion criteria below, the investigator must consult with the appropriate sponsor representative and resolve any issues before enrolling a subject in the study. Waivers are not allowed.

Inclusion Criteria

Each potential subject must satisfy all of the following criteria to be enrolled in the study:

1. Subject must be a man or woman, 18 to 64 years of age, inclusive.

2. Subject must meet Diagnostic and Statistical Manual of Mental Disorders (5th edition) (DSM-5) diagnostic criteria for MDD, without psychotic features, based upon clinical assessment and confirmed by the MINI.

3. Subjects must have current suicidal ideation with intent, confirmed by a "Yes" response to Question B3 [Think (even momentarily) about harming or of hurting or of injuring yourself: with at least some intent or awareness that you might die as a result; or think about suicide (ie, about killing yourself)?] AND Question B10 [Intend to act on thoughts of killing yourself?] obtained from the MINI. Note: the response to B3 must refer to the present, whereas the response to B10 may reflect the past 24 hours. If the screening period is longer than 24 hours, assessment of B3 and B10 of MINI must be repeated prior to randomization to confirm eligibility.

4. In the physician's opinion, acute psychiatric hospitalization is clinically warranted due to subject's imminent risk of suicide.

5. Subject has a MADRS total score of >28 predose on Day 1.

6. As part of standard of care treatment, subject agrees to be hospitalized voluntarily for a recommended period of 5 days (14 days for sites in Austria, Belgium, Czech, France, Lithuania, Poland) after randomization (may be shorter or longer if clinically warranted in the investigator's opinion) and take prescribed noninvestigational antidepressant therapy(ies) for at least the duration of the double-blind treatment phase (Day 25).

7. Subject is comfortable with self-administration of intranasal medication and able to follow instructions provided.

8. Subject must be medically stable on the basis of physical examination, medical history, vital signs, and 12-lead ECG performed at screening. If there are

abnormalities, the subject may be included only if the investigator judges the abnormalities to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the investigator.

Note: Subjects recovering from a recent suicide attempt may be eligible provided they are medically stable.

9. Subject must be medically stable on the basis of clinical laboratory tests performed by the local laboratory at screening. If the results of the serum chemistry panel, hematology, or urinalysis are outside the normal reference ranges, the subject may be included only if the investigator judges the abnormalities or deviations from normal to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the investigator.

   - Incidental exclusionary laboratory values ("incidental" refers to duplicate results from a separate blood sample analyzed at the central laboratory that become available after the subject has satisfied the inclusion and exclusion criteria based on the local laboratory values) will be handled on a case-by-case basis to determine if the subject should be withdrawn from the study.

10. Contraceptive use by men or women should be consistent with local regulations regarding the use of contraceptive methods for subject participating in clinical studies.

    Before randomization, a woman must be either:

    a. Not of childbearing potential defined as:
       - postmenopausal (>45 years of age with amenorrhea for at least 12 months), permanently sterilized (eg, bilateral tubal occlusion/ligation procedures, hysterectomy, bilateral salpingectomy, bilateral oophorectomy); or otherwise be incapable of pregnancy

    b. Of childbearing potential and
       - practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly)

         Examples of highly effective contraceptives include
         - user-independent methods:
           implantable progestogen-only hormone contraception associated with inhibition of ovulation; intrauterine device (IUD); intrauterine hormone-releasing system (IUS); vasectomized partner; sexual abstinence (*sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study drug. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the subject*.)
         - user-dependent methods:

combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, and transdermal; progestogen-only hormone contraception associated with inhibition of ovulation: oral and injectable

Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for subjects participating in clinical studies.

- o agrees to use a highly effective method throughout the study and for at least 6 weeks after the last dose of study drug.

Note: If the childbearing potential changes after start of the study or the risk of pregnancy changes (eg, a woman who is not heterosexually active becomes active), a woman must begin a highly effective method of contraception, as described throughout the inclusion criteria.

11. A woman of childbearing potential must have a negative urine pregnancy test at screening.

12. During the study (ie, from Day 1 of the double-blind phase) and for a minimum of 1 spermatogenesis cycle (defined as approximately 90 days) after receiving the last dose of study drug, a man who is sexually active with a woman of childbearing potential
    - must be practicing a highly effective method of contraception with his female partner from those listed above (see examples of highly effective methods of contraception provided for female subjects).
    - must use a condom if his partner is pregnant.
    - must agree not to donate sperm.

Note: If the childbearing potential changes after start of the study, a female partner of a male study subject must begin a highly effective method of birth control, as described above.

13. Subject must be willing and able to adhere to the prohibitions and restrictions specified in this protocol.

14. Each subject must sign an informed consent form (ICF) indicating that he or she understands the purpose of and procedures required for the study and is willing to participate in the study.

Note: Subjects with acute alcohol intoxication should not be screened (but can be screened once sober).

15. Each subject must sign a separate informed consent form if he or she agrees to provide an optional DNA sample for research (where local regulations permit).

Refusal to give consent for the optional DNA research sample does not exclude a subject from participation in the study.

Exclusion Criteria

Any potential subject who meets any of the following criteria will be excluded from participating in the study:

1. Subject has a current DSM-5 diagnosis of bipolar (or related disorders), antisocial personality disorder, or obsessive compulsive disorder.

2. Subject currently meets DSM-5 criteria for borderline personality disorder.
   - Subjects not meeting full DSM-5 criteria for borderline personality disorder but exhibiting recurrent suicidal gestures, threats, or self-mutilating behaviors should also be excluded.

3. Subject has a current clinical diagnosis of autism, dementia, or intellectual disability.

4. Subject has a current or prior DSM-5 diagnosis of a psychotic disorder, or MDD with psychotic features.

5. Subject meets the DSM-5 severity criteria for moderate or severe substance or alcohol use disorder (except for nicotine or caffeine) within the 6 months (12 months for some EU countries) before screening.
   - A history (lifetime) of ketamine, phencyclidine (PCP), lysergic acid diethylamide (LSD), or 3, 4-methylenedioxy-methamphetamine (MDMA) hallucinogen-related use disorder is exclusionary.

6. Subject has any of the following conditions:
   - a history or current signs and symptoms of liver or renal insufficiency
   - clinically significant cardiac (including unstable coronary artery disease and congestive heart failure, tachyarrhythmias and recent myocardial infarction) or vascular, pulmonary, gastrointestinal, endocrine (including uncontrolled hyperthyroidism), neurologic (including current or past history of seizures except uncomplicated childhood febrile seizures with no sequelae), hematologic, rheumatologic, or metabolic (including severe dehydration/hypovolemia) disease.

7. Subject has uncontrolled hypertension (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg) despite diet, exercise or a stable dose of antihypertensive treatment for at least 2 weeks at screening; or any past history of hypertensive crisis.
   - Subjects with conditions in which the elevation of blood pressure could be a serious risk (including unstable heart failure, severe cardiovascular disease, recent cerebral injury, increased intracranial pressure / intracranial mass lesion, intracranial bleeding or acute stroke, untreated glaucoma or perforating eye injury) are excluded.

- An abnormal blood pressure value at screening can be repeated once after 5 minutes of relaxation for subject eligibility. On Day 1 of the double-blind phase prior to randomization, a supine or semi-supine systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg is exclusionary.

8. Subject has a positive urine test result(s) for phencyclidine (PCP), cocaine, or amphetamines (inclusive of amphetamine, methamphetamine [mAMP], and 3, 4-methylenedioxy-methamphetamine [MDMA]) at screening.
   - Subjects who have a positive test due to the appropriate use of prescribed opiates, benzodiazepines, or barbiturates may be eligible for study participation per clinician judgment. In addition, subjects who have a positive test for opiates, benzodiazepines, or barbiturates used without a prescription, may be considered eligible per clinician judgment and in consultation with the sponsor's medical monitor. Subjects known to be using heroin should be excluded from the study.
   - Subjects who have a positive test due to opiates, benzodiazepines, or barbiturates taken in a suicide attempt (eg, overdose) may be eligible for study participation per clinician judgment and in consultation with the sponsor's medical monitor.
   - Subjects, who have a positive test result at screening due to prescribed psychostimulants (eg. amphetamine, methylphenidate) that are permitted during the study in accordance with Attachment 1, are eligible for study participation.

9. Subject has a history of malignancy within 5 years before screening (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix, or malignancy that in the opinion of the investigator, with concurrence with the sponsor's medical monitor, is considered to have minimal risk of recurrence).

10. Subject has any anatomical or medical condition that, per the investigator's clinical judgment based on assessment, may impede delivery or absorption of intranasal study drug.

11. Subject has known allergies, hypersensitivity, intolerance or contraindications to esketamine or ketamine or its excipients (refer to Investigator's Brochure for esketamine, Summary of Product Characteristics, US prescribing information).

12. Subject has taken any disallowed therapy(ies) as noted in Section 8, Prestudy and Concomitant Therapy, and Attachment 1.

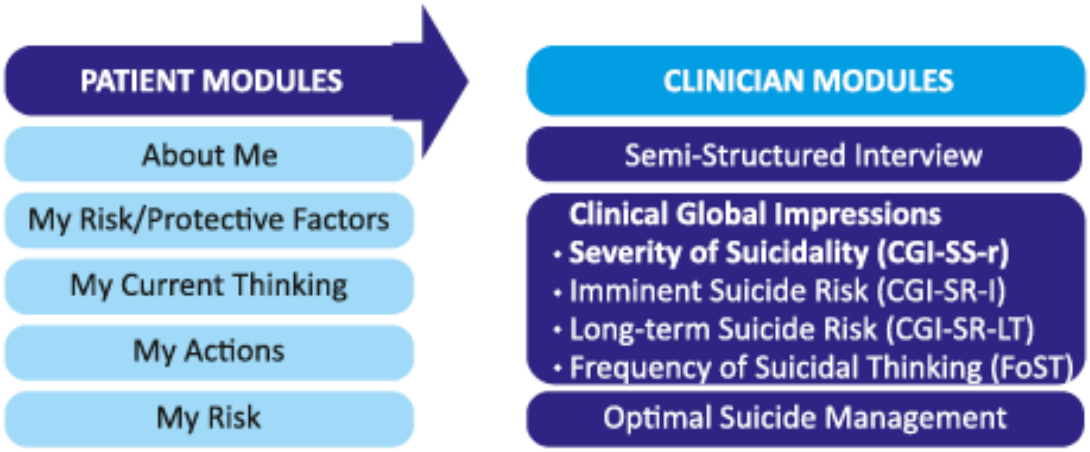
13. Subject has received an investigational drug (including esketamine, ketamine, or investigational vaccines) or used an invasive investigational medical device within 60 days before the planned first dose of study drug or is currently enrolled in an investigational study or was previously enrolled in this study or the Sponsor's other studies in this population, 54135419SUI3001 and ESKETINSUI2001.

14. Subject is a woman who is pregnant, breast-feeding, or planning to become pregnant while enrolled in this study or within 3 months after the last dose of study drug.

15. Subject has any situation or condition for which, in the opinion of the investigator, participation would not be in the best interest of the subject (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

16. Subject is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.
    NOTE: Investigators should ensure that all study enrollment criteria have been met at screening.

Supplementary Figure 1. Suicide Ideation and Behavior Assessment Tool (SIBAT) Structure



MedDRA Preferred Terms of Adverse Events Potentially Related to Suicidality

completed suicide, depression suicidal, intentional overdose, intentional self-injury, multiple drug overdose intentional, poisoning deliberate, self-injurious behavior, self-injurious ideation, suicidal behavior, suicidal ideation, and suicide attempt

Supplementary Table 1. Standard-of-Care Antidepressant Medications by Treatment Group During the Double-Blind Treatment Phase

	Number (%) of Patients		
	Placebo + Standard-of-Care N = 113	**Esketamine 84 mg + Standard-of-Care N = 114**	**All Patients N = 227**
Quetiapine	30 (26.5)	34 (29.8)	64 (28.2)
Venlafaxine	36 (31.9)	28 (24.6)	64 (28.2)
Escitalopram	23 (20.4)	16 (14.0)	39 (17.2)
Duloxetine	13 (11.5)	20 (17.5)	33 (14.5)
Sertraline	15 (13.3)	16 (14.0)	31 (13.7)
Mirtazapine	13 (11.5)	16 (14.0)	29 (12.8)
Aripiprazole	14 (12.4)	11 (9.6)	25 (11.0)
Bupropion	10 (8.8)	14 (12.3)	24 (10.6)
Desvenlafaxine	11 (9.7)	10 (8.8)	21 (9.3)
Trazadone	13 (11.5)	4 (3.5)	17 (7.5)
Lithium	8 (7.1)	6 (5.3)	14 (6.2)
Fluoxetine	4 (3.5)	9 (7.9)	13 (5.7)
Olanzapine	6 (5.3)	6 (5.3)	12 (5.3)
Clomipramine	3 (2.7)	7 (6.1)	10 (4.4)
Vortioxetine	7 (6.2)	1 (0.9)	8 (3.5)

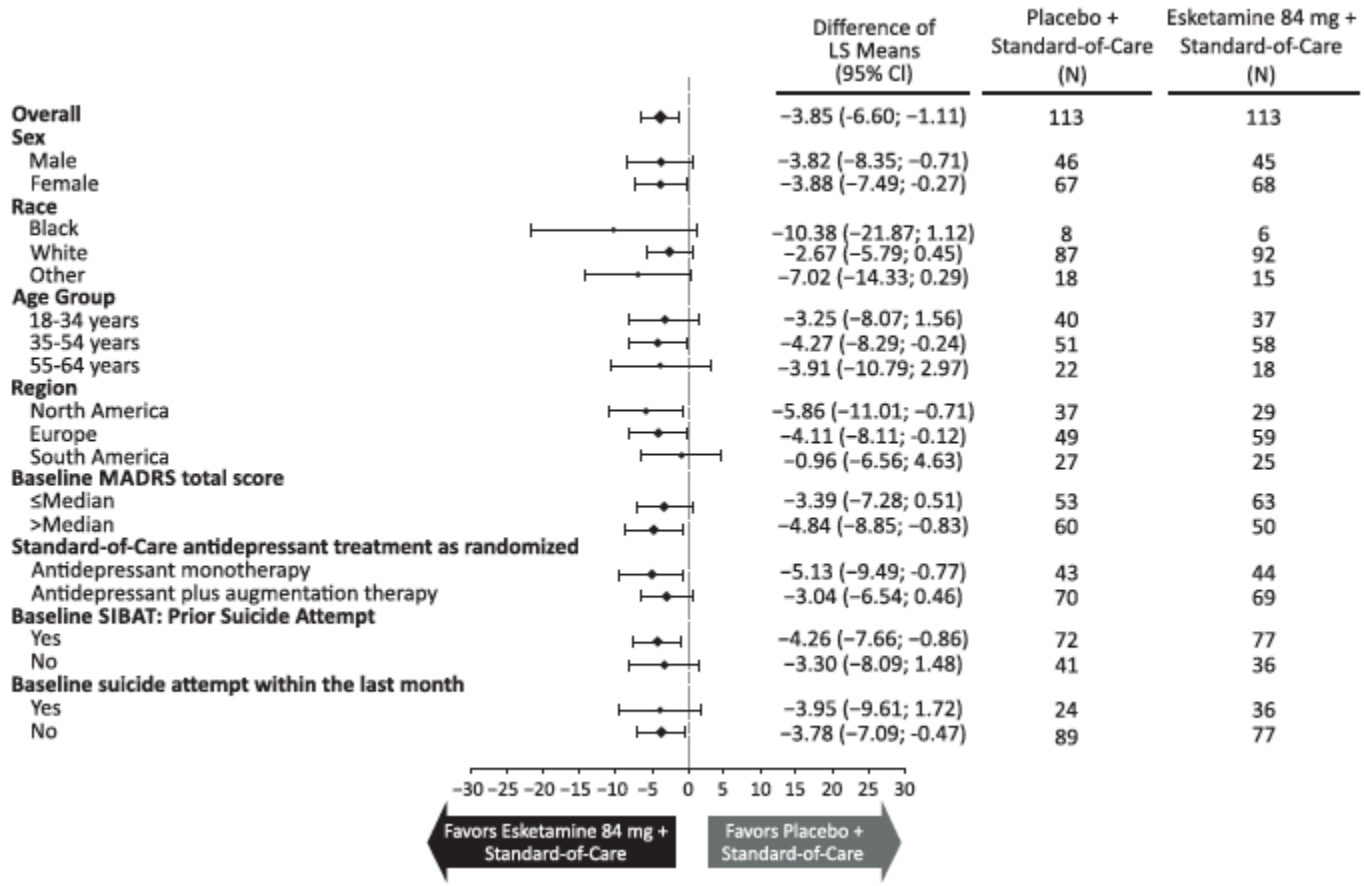
Notes: Incidence ≥5% in either treatment group; medications presented in descending order of incidence based on combined usage across the treatment groups. The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.
In this study, 1 patient (0.9%) in the placebo + standard-of-care group and 2 patients (1.8%) in the esketamine +standard-of-care group used lamotrigine during the double-blind treatment phase.

Supplementary Table 2. Concomitant Benzodiazepines Taken During the Double-Blind Treatment Phase

	Number (%) of Patients		
	Placebo + Standard-of-Care N = 113	**Esketamine 84 mg + Standard-of-Care N = 114**	**All Patients N = 227**
Total patients	70 (61.9)	83 (72.8)	153 (67.4)
Clonazepam	31 (27.4)	36 (31.6)	67 (29.5)
Lorazepam	24 (21.2)	33 (28.9)	57 (25.1)
Diazepam	11 (9.7)	12 (10.5)	23 (10.1)
Alprazolam	8 (7.1)	11 (9.6)	19 (8.4)
Clorazepic acid	1 (0.9)	3 (2.6)	4 (1.8)
Estazolam	1 (0.9)	2 (1.8)	3 (1.3)
Nitrazepam	1 (0.9)	2 (1.8)	3 (1.3)
Prazepam	2 (1.8)	1 (0.9)	3 (1.3)
Oxazepam	0	2 (1.8)	2 (0.9)
Bromazepam	1 (0.9)	0	1 (0.4)
Lormetazepam	1 (0.9)	0	1 (0.4)
Midazolam	0	1 (0.9)	1 (0.4)

Notes: Benzodiazepines are presented in descending order based on combined usage across the treatment groups. The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.

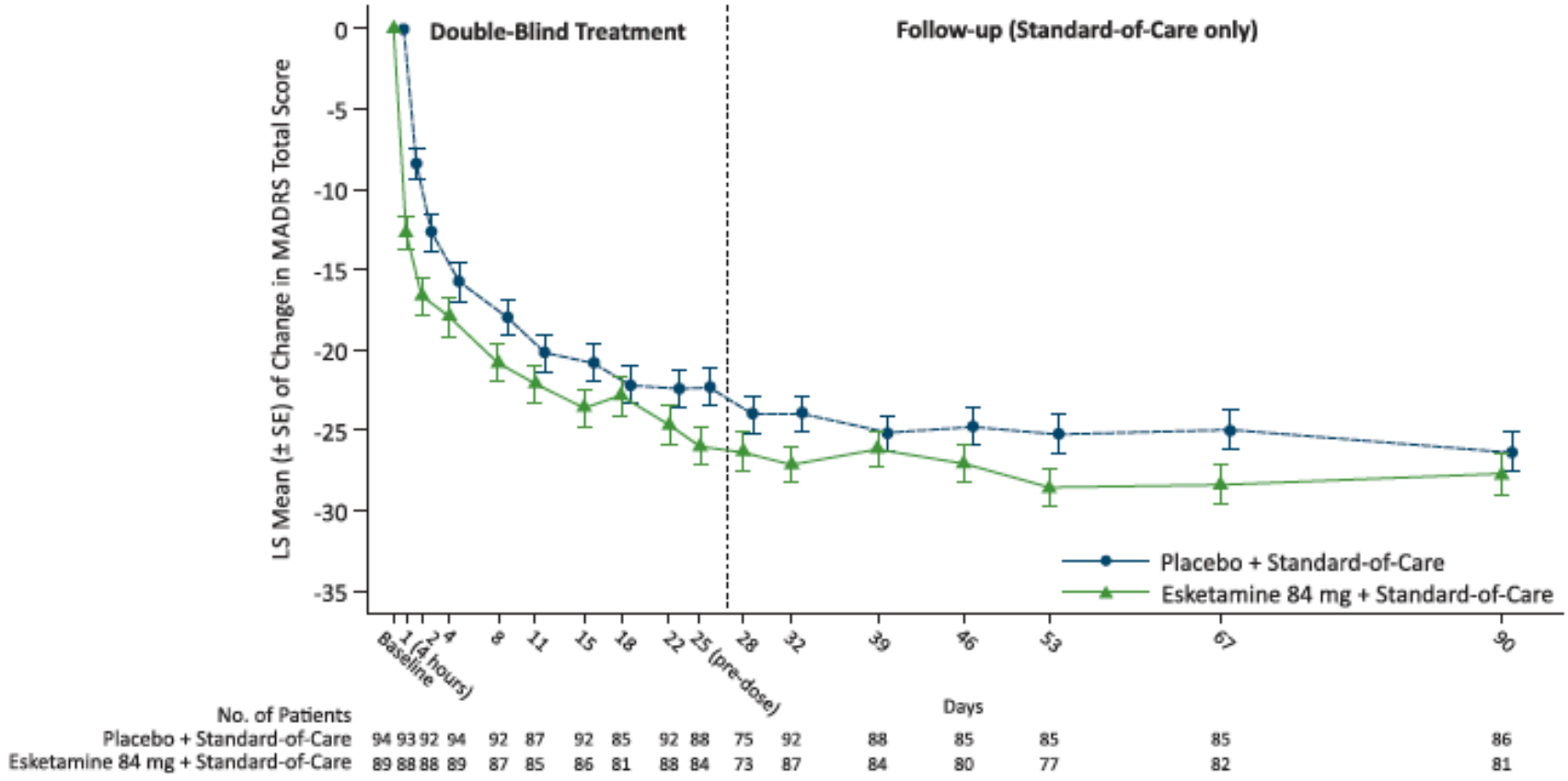
Supplementary Figure 2. Forest Plot for MADRS Total Score: Least Squares Mean Treatment Difference of Change From Baseline (95% CI) to 24 Hours Post-First Dose by Subgroup (ANCOVA LOCF)



ANCOVA = analysis of covariance, CI = confidence interval, LOCF = last observation carried forward, LS = least square, MADRS = Montgomery-Asberg Depression Rating Scale; SIBAT = Suicide Idedation and Behavior Assessment Tool

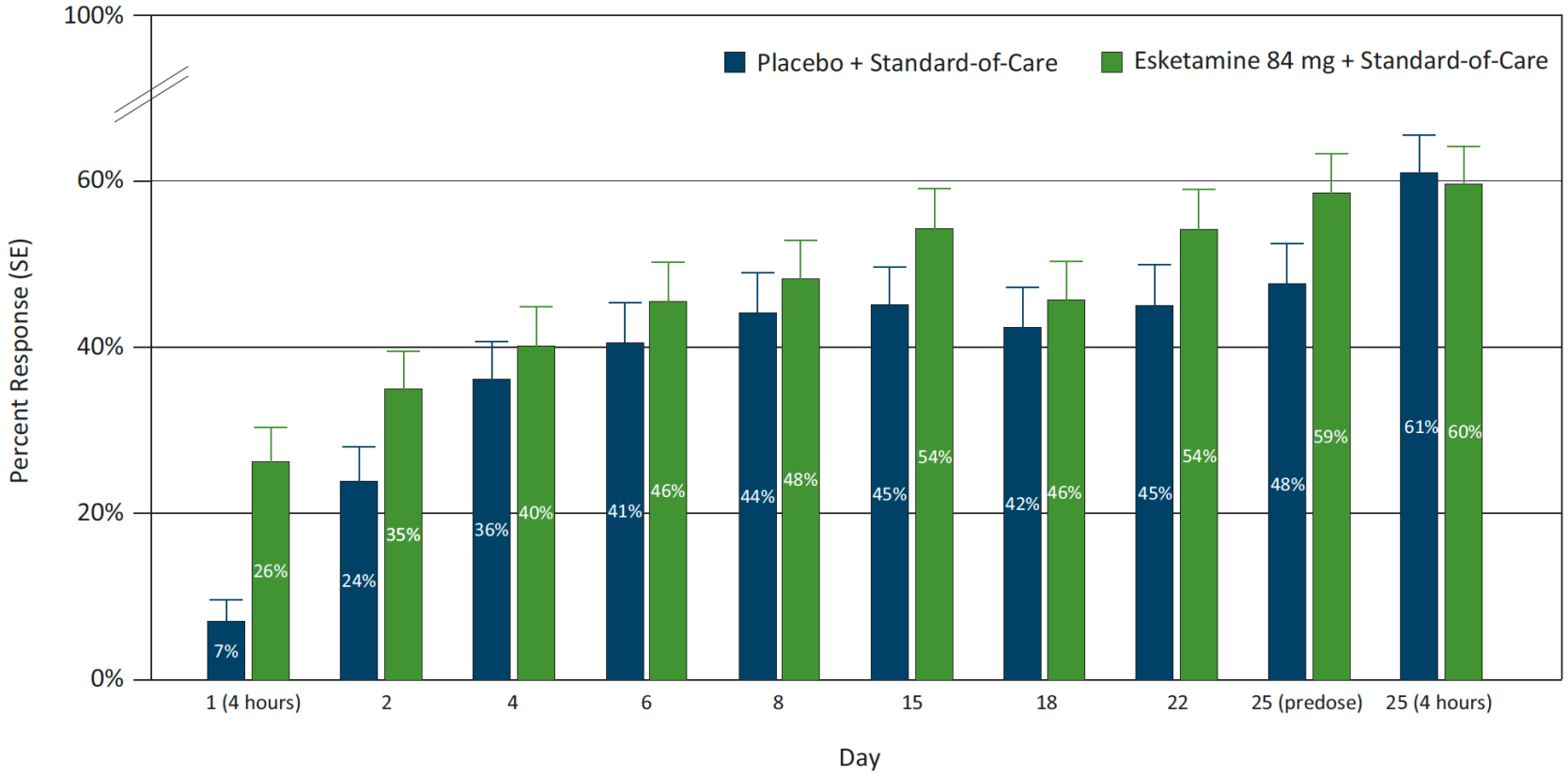
Notes: Negative change in score indicates improvement.
The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.

Supplementary Figure 3. Least-Squares Mean Changes (± SE) from Baseline for MADRS Total Score During the Double-Blind Treatment and Follow-up Phases (MMRM; Observed Cases)



MADRS = Montgomery-Asberg Depression Rating Scale; MMRM = mixed-effects model using repeated measures; SE = standard error
Notes: Negative change in score indicates improvement.
During the follow-up phase, these were patients formerly treated with placebo and patients formerly treated with esketamine.
The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.

Supplementary Figure 4. MADRS Response Rate Over Time During the Double-Blind Treatment Phase

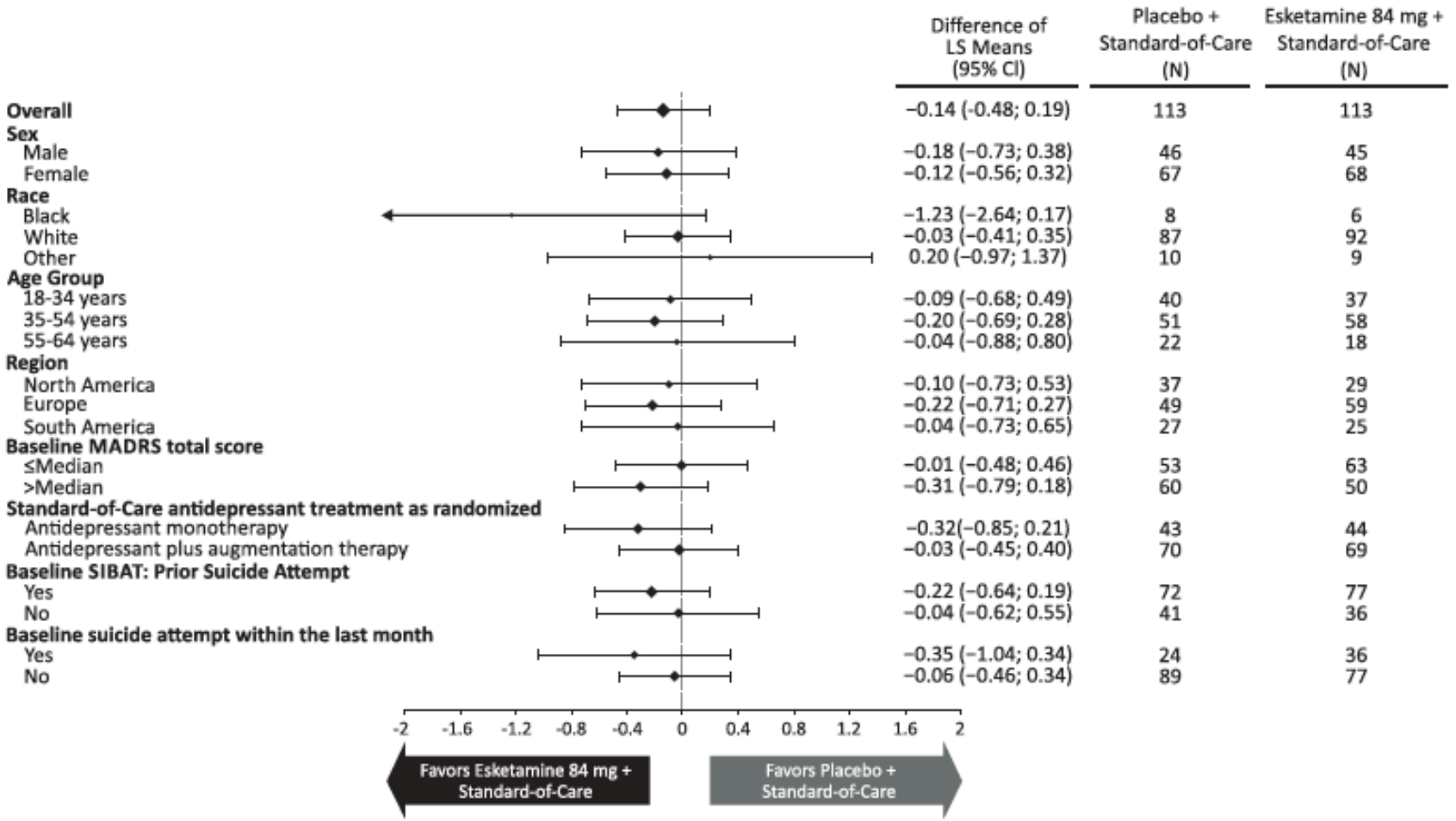


MADRS = Montgomery-Asberg Depression Rating Scale

Notes: Response was based on ≥ 50% improvement in a MADRS total score. Patients who did not meet such criterion or discontinued prior to the time point for any reason were not considered a responder.

The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.

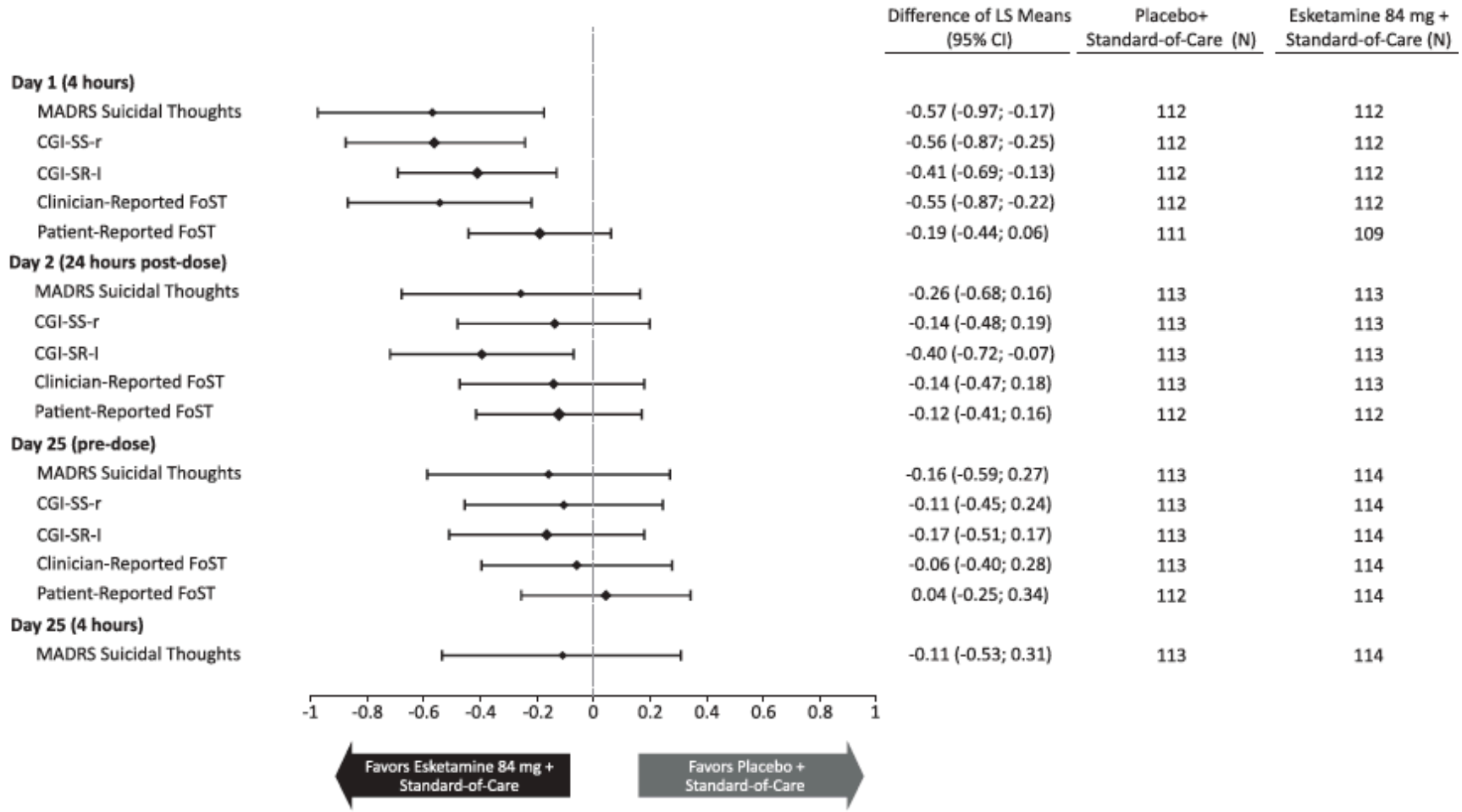
Supplementary Figure 5. Forest Plot for CGI-SS-r Score: Least Squares Mean Treatment Difference of Change from Baseline (95% CI) to 24 Hours Post-First Dose by Subgroup (ANCOVA LOCF)



ANCOVA = analysis of covariance, CGI-SS-r = Clinical Global Impression – Severity of Suicidality – Revised, CI = confidence interval, LOCF = last observation carried forward, LS = least square

Notes: The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.
CGI-SS-r rated from 0 (normal, not at all suicidal) to 6 (among the most extremely suicidal patients).

Supplementary Figure 6. Treatment Difference on CGI-SS-r and Other Suicidality Indices During the Double-Blind Treatment Phase (ANCOVA LOCF)



ANCOVA = analysis of covariance, CGI-SR-I = Clinical Global Impression–Imminent Suicide Risk; CGI-SS-r, Clinical Global Impression–Severity of Suicidality–revised; CI = confidence interval; LOCF = last observation carried forward, LS = least squares, FoST, Frequency of Suicidal Thinking; MADRS, Montgomery-Åsberg Depression Rating Scale

Notes: The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.

Supplementary Table 3. Summary of Most Frequently Reported[a] Adverse Events During the Follow-up Phase

	Number (%) of Patients	
	Placebo + Standard-of-Care[c] N = 94	**Esketamine 84 mg[b] + Standard-of-Care[c] N = 89**
Patients with ≥1 adverse events	55 (58.5)	53 (59.6)
Anxiety	9 (9.6)	8 (9.0)
Insomnia	7 (7.4)	8 (9.0)
Headache	10 (10.6)	7 (7.9)
Suicidal ideation	7 (7.4)	5 (5.6)
Diarrhea	5 (5.3)	3 (3.4)

a. Most frequently reported is defined as ≥5% of patients in either treatment group. Events are presented in descending order in the esketamine group.
b. Includes patients who had their dose reduced due to tolerability issues.
c. This is the treatment assignment during the double-blind phase. During the follow-up phase, patients were only treated by standard-of-care antidepressant therapy.

Supplementary Table 4. Summary of Treatment-Emergent Serious Adverse Events[a] During the Double-Blind Phase

	Number (%) of Patients	
	Placebo + Standard-of-Care N = 113	**Esketamine 84 mg[b] + Standard-of-Care N = 114**
Patients with ≥1 serious adverse events	6 (5.3)	5 (4.4)
Suicide attempt	3 (2.7)	3[c] (2.6)
Suicidal ideation	2 (1.8)	1 (0.9)
Depersonalization/derealization disorder	0	1 (0.9)
Arrhythmia	1 (0.9)	0
Depression	1 (0.9)	0
Pericardial effusion	1 (0.9)	0
Pneumothorax	1 (0.9)	0

a. Events are presented in descending order in the esketamine group.
b. Includes patients who had their dose reduced due to tolerability issues.
c. In addition, 1 patient who discontinued from the study after the first dose (due to the AE of blood pressure increased), attempted suicide on what would have been day 26. The patient had a history of suicide attempt.

Supplementary Table 5. Summary of Serious Adverse Events[a] During the Follow-up Phase

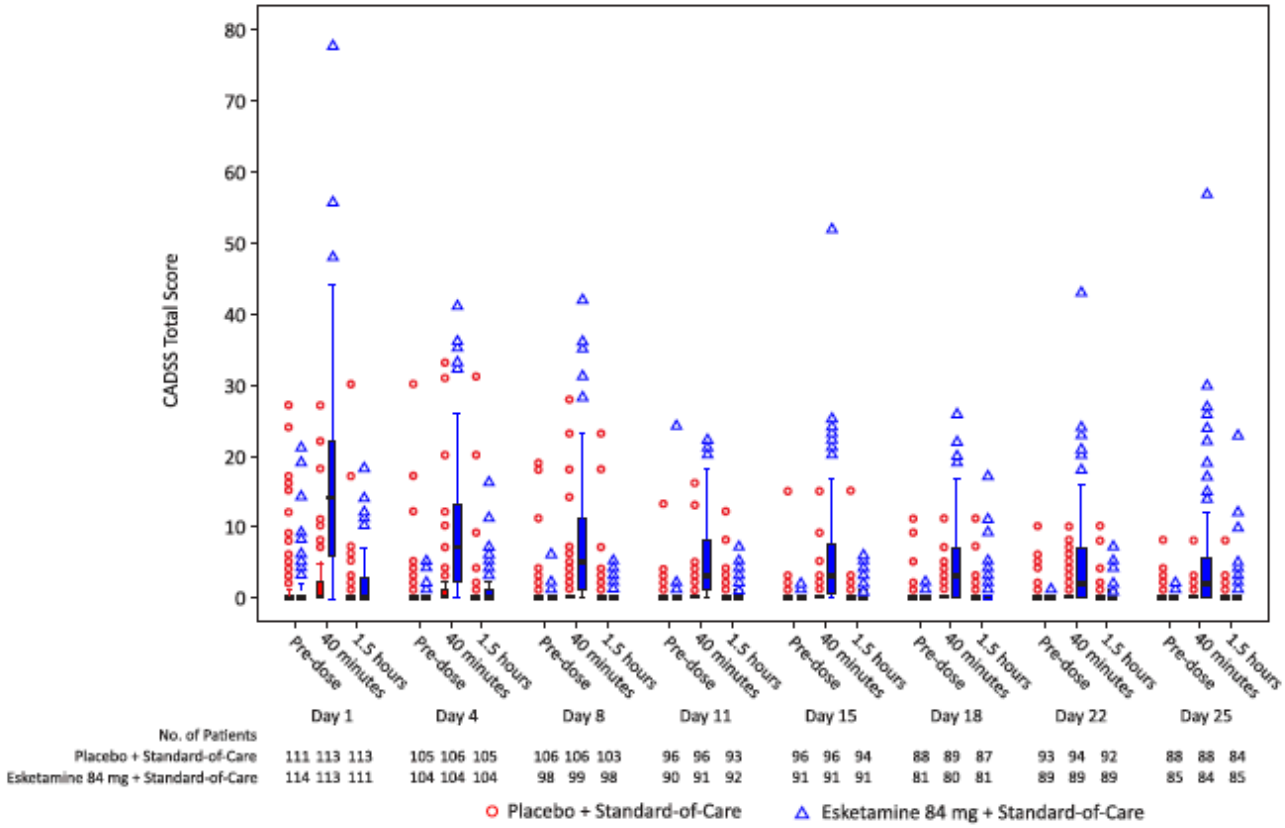
	Number (%) of Patients	
	Placebo + Standard-of-Care[c] N = 94	Esketamine 84 mg[b] + Standard-of-Care[c] N = 89
Patients with ≥1 serious adverse events	12 (12.8)	9 (10.1)
Suicide attempt	1 (1.1)	4[d] (4.5)
Suicidal ideation	3 (3.2)	3 (3.4)
Acute stress disorder	0	1 (1.1)
Hemothorax	0	1 (1.1)
Major depression	0	1 (1.1)
Depression suicidal	2 (2.1)	0
Encephalopathy	1 (1.1)	0
Erysipelas	1 (1.1)	0
Homicidal ideation	1 (1.1)	0
Overdose	1 (1.1)	0
Papillary thyroid cancer	1 (1.1)	0
Pyelonephritis	1 (1.1)	0
Staphylococcal bacteremia	1 (1.1)	0

a. Events are presented in descending order in the esketamine group.
b. Includes patients who had their dose reduced due to tolerability issues.
c . This is the treatment assignment during the double-blind phase. During the follow-up phase, patients were only treated by standard-of-care antidepressant therapy.
d. Events occurred on study days 30, 36, 49, and 86.

Adverse Events Leading to Discontinuation of Study Drug

Twelve patients discontinued intranasal study drug prematurely due to an adverse event: 9 patients (7.9%) in the esketamine plus standard-of-care group (due to: dissociation [2 patients], dizziness postural, blood pressure increased, paresthesia oral, depersonalization/derealization disorder [1 patient each], nausea and vomiting [both events in 1 patient], depersonalization/ derealization disorder, nausea, and throat irritation (all 3 events in 1 patient), nasal discomfort and dyspepsia [both events in 1 patient]) and 3 patients (2.7%) in the placebo plus standard-of-care group (due to: pericardial effusion and depression suicidal [1 patient each] and arrhythmia and pneumothorax [both events in 1 patient]).

Suplementary Figure 7. CADSS Total Score Box Plot Over Time During Double-Blind Treatment



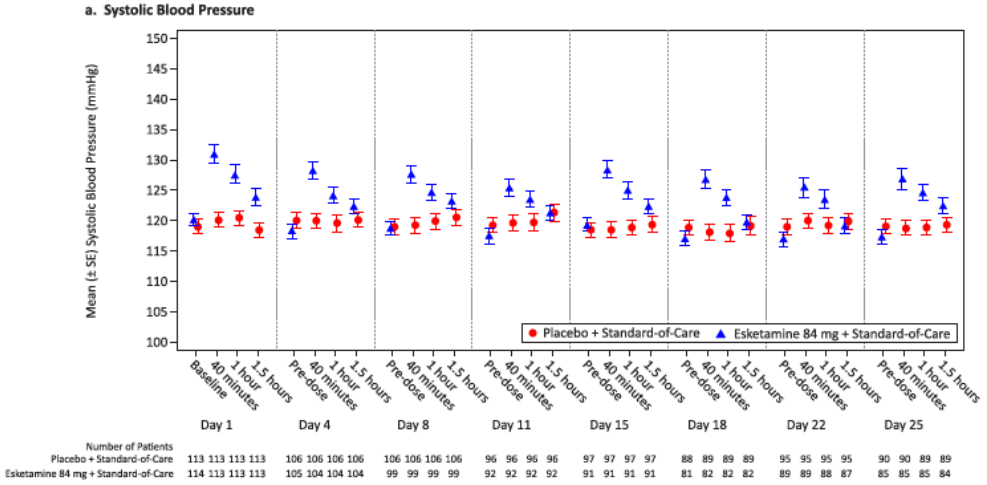
CADSS = Clinician-administered Dissociative States Scale

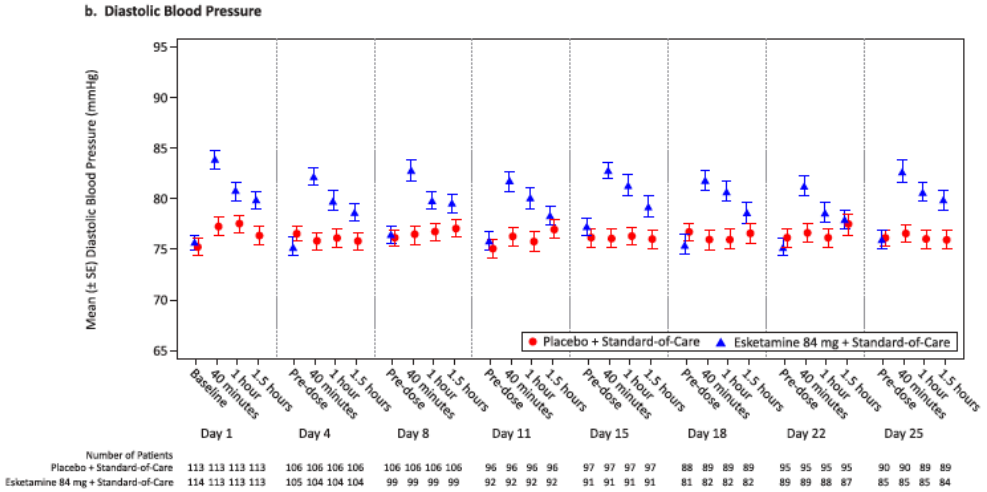
Notes: CADSS total score ranges from 0 to 92; a higher score indicates a more severe condition. Any CADSS items scored zero at 40 minutes postdose did not need to be repeated at 1.5 hours postdose. The zero scores at 40 minutes were carried forward to 1.5 hours.

The lower boundary of the box is the 25th percentile, the higher boundary is the 75th percentile, and the solid line within the box marks the median. Whiskers below and above the box indicate the 1.5*interquartile range below the lower boundary (or the smallest value) and 1.5*interquartile range above the higher boundary (or the largest value). Outlying data points are extreme values.

The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.

Suplementary Figure 8. Mean (± SE) Systolic and Diastolic Blood Pressure Over Time During Double-Blind Treatment





Notes: The esketamine 84 mg group includes patients who had their dose reduced due to tolerability issues.