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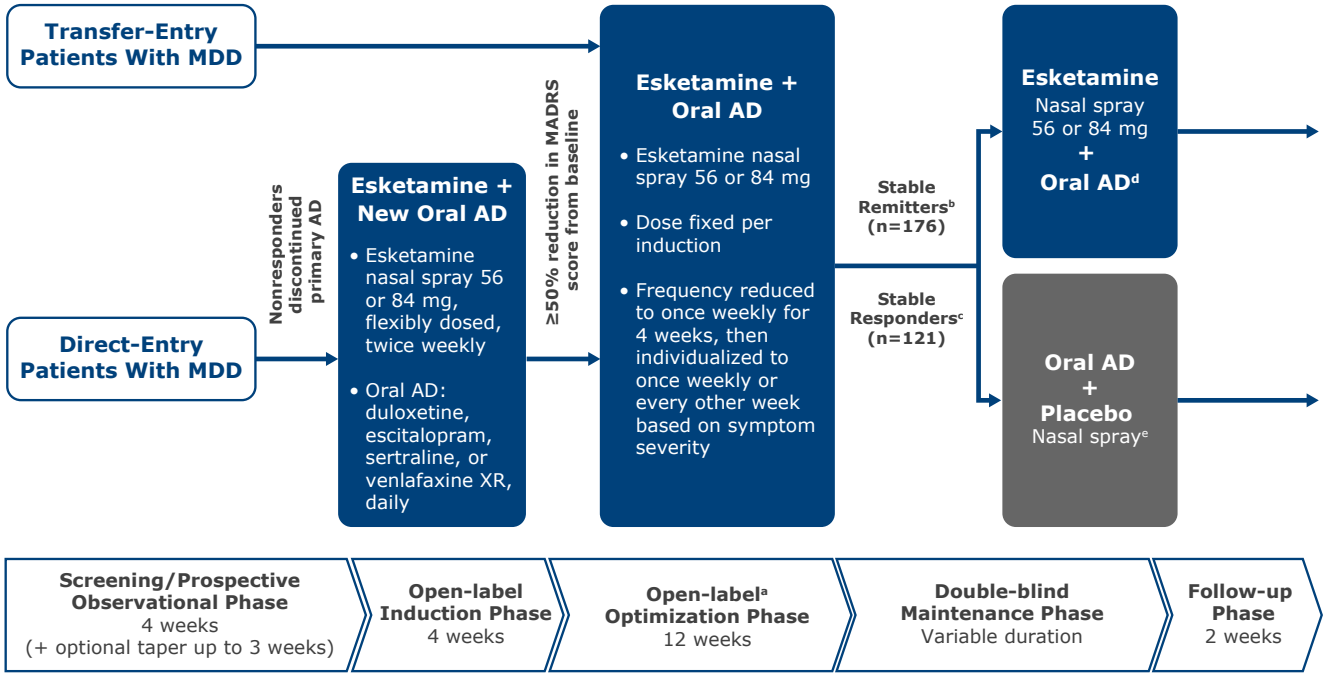
- SUSTAIN-1 (NCT02493868) was a phase 3, double-blind, active-controlled, randomized withdrawal, maintenance-of-effect, multicenter study conducted in 99 sites across 16 countries in patients.[1]



[a]Double-blind for transfer-entry patients (oral AD + either esketamine or placebo).
[b]MADRS score ≤12 for ≥3 of the last 4 weeks, with 1 MADRS score >12 or 1 missing assessment permitted at week 13 or 14.
[c]≥50% reduction in MADRS score from baseline in the past 2 weeks, without remission.
[d]Stable remitters, n=90; stable responders, n=62.
[e]Stable remitters, n=86; stable responders, n=59.

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Inclusion Criteria[1]	**Exclusion Criteria**[1]
Direct-entry patients: • Age 18-64 years • Single-episode (≥2 years) or recurrent MDD, without psychotic features, per DSM-5 and clinical assessment, confirmed by MINI • IDS-C_{30} score ≥34 and MADRS score ≥28 • Nonresponse to ≥1 but ≤5 oral ADs of adequate dose, duration, and adherence in current MDD episode, per MGH-ATRQ and documented records, and taking a different oral AD for ≥2 previous weeks at or above the minimum therapeutic dose • Current MDD episode, depression symptom severity, and AD response in the current depressive episode, must be confirmed using a Site Independent Qualification Assessment **Transfer-entry patients:** • Completed and demonstrated response (≥50% reduction from baseline in the MADRS score) after double-blind induction phase from two short-term studies[4,5]	• Homicidal ideation/intent, or suicidal ideation with some intent to act, for ≤6 months, per the investigator's judgment or per C-SSRS or history of suicidal behavior within the past year • Bipolar or related disorders; comorbid OCD; intellectual disability; or borderline, antisocial, histrionic, or narcissistic personality disorder • History of uncontrolled hypertension or certain cardiovascular conditions; seizures; or moderate or severe substance or alcohol use disorder per DSM-5, in the past 6 months • Nonresponse in the current episode to esketamine or ketamine, to all 4 of the oral AD treatment options, or an adequate course of ECT • Received vagal nerve stimulation or deep brain stimulation in the current episode

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Primary Efficacy Endpoint

- Time to relapse among stable remitters during the maintenance phase.[1]
  - Relapse was defined as MADRS score ≥22 for 2 consecutive assessments separated by 5-15 days or hospitalization for worsening depression, suicide attempt, suicide prevention or completed suicide, or any other clinically relevant event suggestive of relapse.[1]
  - Relapse was assessed by a relapse adjudication committee on weeks 1, 2, and 4 during screening and observation and weekly during the induction, optimization, maintenance, and follow-up phases.[7]

Secondary Efficacy Endpoint[1]

- Time to relapse among stable responders without remission during the maintenance phase.

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- Demographics and baseline characteristics were similar across treatment arms.[1]

Characteristic	Stable Remitters		Stable Responders	
	Esketamine + AD (n=90)	AD + Placebo (n=86)	Esketamine + AD (n=62)	AD + Placebo (n=59)
Age, years, mean (SD)	45.4 (12.12)	46.2 (11.16)	47.2 (11.00)	46.7 (9.76)
Sex, female, n (%)	58 (64.4)	59 (68.6)	38 (61.3)	42 (71.2)
Race, n (%)				
Black	4 (4.4)	6 (7.0)	2 (3.2)	1 (1.7)
White	80 (88.9)	76 (88.4)	57 (91.9)	55 (93.2)
Other	3 (3.3)	2 (2.3)	3 (4.8)	3 (5.1)
Duration of current episode, weeks, mean (SD)	112.2 (171.30)	110.5 (147.41)	121.6 (193.85)	141.8 (254.43)
MADRS score, mean (SD)	37.4 (5.20)	37.6 (4.66)	40.1 (5.56)	38.9 (4.92)
Number of previous AD medications, n (%)				
≤2	71 (78.9)	62 (73.8)	41 (66.1)	34 (57.6)
>2	19 (21.1)	22 (26.2)	21 (33.9)	25 (42.4)
Class of oral AD, n (%)				
SNRI	62 (68.9)	58 (67.4)	35 (56.5)	36 (61.0)
SSRI	28 (31.1)	28 (32.6)	27 (43.5)	23 (39.0)

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Treatment Exposure[1]

- The median exposure to the study drug was as follows:

Median Study Drug Exposure, Weeks	Esketamine + AD	AD + Placebo
Stable remitters[a]	17.7	10.2
Stable responders[b]	19.4	10.1

[a]Stable remission was defined as an MADRS score ≤12 for ≥3 of the last 4 weeks, with 1 MADRS score >12 or 1 missing assessment permitted at week 13 or 14.

[b]Stable response was defined as a ≥50% reduction in MADRS score from baseline in the past 2 weeks, without remission.

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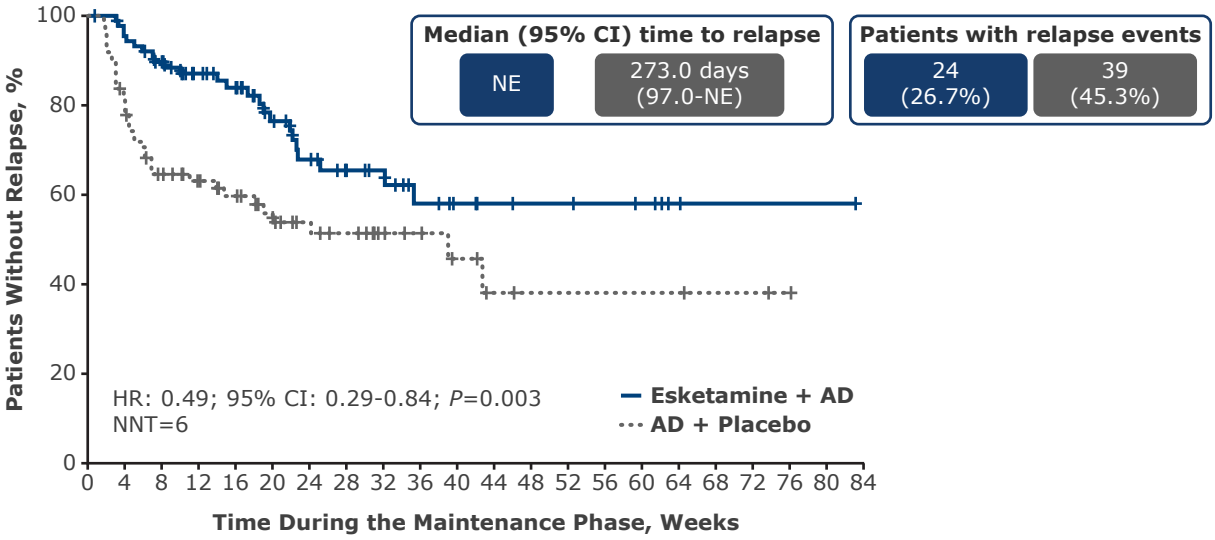
- Among stable remitters,[a] esketamine + AD significantly delayed relapse compared to AD + placebo and reduced the risk of relapse by 51%.[1]



No. at risk

Esketamine + AD	90	84	74	58	53	39	31	25	20	14	10	8	7	7	6	5	2	1	1	1	0
AD + Placebo	86	69	52	41	34	28	22	19	12	10	7	4	3	3	3	3	3	2	2	1	0	0

- Among stable remitters, 26.7% (24/90) of patients in the esketamine + AD group and 45.3% (39/86) in the AD + placebo group relapsed; hospitalization was the reason for relapse in 12.5% (3/24) and 0% of patients in the 2 groups, respectively.[8]

Censored Patients – Discontinuation (Maintenance Phase)

[a]Stable remission was defined as MADRS score ≤12 for ≥3 of the last 4 weeks, with 1 MADRS score >12 or 1 missing assessment permitted at week 13 or 14.

Censored Patients – Discontinuation (Maintenance Phase)

- Censoring was done for patients who remained relapse free at the end of the study (after the defined number of relapse events occurred) or who withdrew early without relapse in the maintenance phase.[1]
- Thirteen patients (stable remission, n=8; stable response, n=5) in the esketamine + AD group and 12 patients (stable remission, n=9; stable response, n=3) in the AD + placebo group were censored because they discontinued the maintenance phase before having a relapse and before the end of the study.[1]
- Treatment withdrawal in the maintenance phase was due to:[8]

Esketamine + AD	AD + Placebo
○ Withdrawal by subject, n=5 ○ Other, n=4 ○ AE, n=1 ○ Lost to follow-up, n=1 ○ Pregnancy, n=1 ○ Protocol violation, n=1	○ Other, n=5 ○ Withdrawal by subject, n=4 ○ AE, n=2 ○ Noncompliance with study drug, n=1

AD, antidepressant; AE, adverse event.

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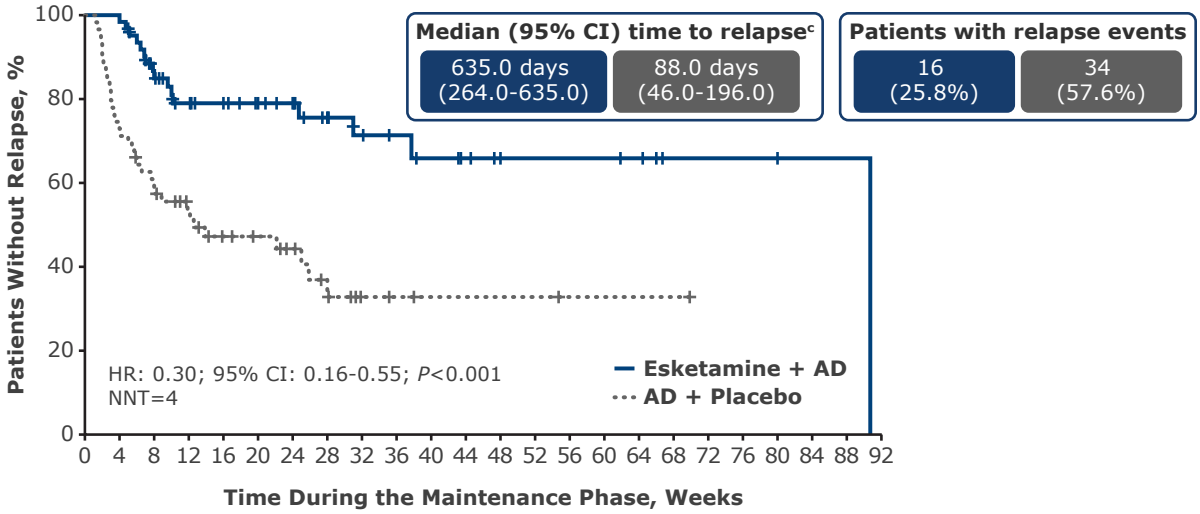
Secondary Efficacy Endpoint[1]

- Among stable responders,[a] esketamine + AD significantly delayed relapse compared to AD + placebo and reduced the risk of relapse by 70%; among the 50 patients who relapsed, there were no hospitalizations in either group.[1,8]
- There were fewer relapse events in stable responders (n=16) vs stable remitters[b] (n=24) who stayed on esketamine + AD; however, the percentage of relapses was similar (25.8% vs 26.7%, respectively) between the groups.[1]
- A higher percentage of relapse events was noted in stable responders vs stable remitters who discontinued esketamine and switched to placebo nasal spray (57.6% vs 45.3%); this is believed to be because this patient population was more vulnerable to relapse due to the fact that they had not achieved stable remission.[1,3]



No. at risk

Esketamine + AD	62	62	49	38	35	31	26	20	15	13	11	9	7	6	6	6	5	2	2	2	2	1	1	0
AD + Placebo		59	44	35	26	19	17	13	9	4	3	2	2	2	1	1	1	1	0	0	0	0	0	0

[a]Stable response was defined as a ≥50% reduction in MADRS score from baseline in the past 2 weeks, without remission.

[b]Stable remission was defined as an MADRS score ≤12 for ≥3 of the last 4 weeks, with 1 MADRS score >12 or 1 missing assessment permitted at week 13 or 14.

[c]The median time to relapse for esketamine + AD should be interpreted with caution, as it is influenced by a single patient who participated in the maintenance phase beyond week 88 and relapsed prior to the end of the study.[9]

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- The **most common AEs** in the esketamine + AD arm (≥20%) during the maintenance phase included dysgeusia, vertigo, dissociation, somnolence, and dizziness and were more frequent than in the AD + placebo arm.[1]
- Most AEs were **mild to moderate** in severity, observed after dosing, and resolved on the same day.[1]
- No fatal events were reported during the study.[1]
- Study drug-related **SAEs** were reported in 6 patients in the esketamine + AD arm only during the induction phase and included the following:[1]
  - Autonomic nervous system imbalance
  - Disorientation
  - Lacunar stroke
  - Hypothermia
  - Sedation
  - Simple partial seizures
  - Suicidal ideation
- **Treatment discontinuation** due to AEs during the maintenance phase are listed below:[1]
  - **Esketamine + AD**: 4 (2.6%) patients discontinued treatment due to worsening depression (n=3), and anxiety and transient confusional state (n=1).
  - **AD + placebo**: 3 (2.1%) patients discontinued treatment due to worsening depression.

TEAEs in the Maintenance Phase in ≥10% Patients in Either Treatment Arm

TEAEs in the Maintenance Phase in ≥10% Patients in Either Treatment Arm[1]

Event, n (%)	Esketamine + AD (n=152)	AD + Placebo (n=145)
Dysgeusia	41 (27.0)	10 (6.9)
Vertigo	38 (25.0)	8 (5.5)
Dissociation	35 (23.0)	0
Somnolence	32 (21.1)	3 (2.1)
Dizziness	31 (20.4)	7 (4.8)
Headache	27 (17.8)	14 (9.7)
Nausea	25 (16.4)	1 (0.7)
Vision blurred	24 (15.8)	1 (0.7)
Hypoesthesia oral	20 (13.2)	0

AD, antidepressant; TEAE, treatment-emergent adverse event.

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Transient Blood Pressure Increases[1]

- The increases occurred after esketamine treatment, typically peaked at 40 minutes postdose, and generally returned to the predose range by 1.5 hours postdose.
- Treatment-emergent transient hypertension during maintenance is summarized below:

Blood Pressure	Esketamine + AD	AD + Placebo
Systolic blood pressure ≥180 mmHg, n (%)	1 (0.7)	0
Diastolic blood pressure ≥110 mmHg, n (%)	2 (1.3)	0

Suicidal Ideation[1]

- The proportion of patients who reported no suicidal ideation or behavior at baseline (C-SSRS score=0) and a higher postbaseline C-SSRS score of ≥1 is summarized below:

Higher Postbaseline C-SSRS Score of ≥1, n (%)	Esketamine + AD	AD + Placebo
Induction phase	42 (11.6)	
Optimization phase	22 (5.7)	
Maintenance phase	3 (2.4)	6 (4.5)

- Patients experiencing relapse did not have a significant elevation in C-SSRS scores.
- Treatment-emergent suicidal behavior was not observed in either arm.

Present-State Dissociative Symptoms[1]

- Per the CADSS, symptoms were observed shortly after the esketamine dose, peaked at 40 minutes, generally resolved by 1.5 hours postdose, and attenuated with repeated dosing.
- Events or symptoms of psychosis were not observed.

Withdrawal Syndrome[1]

- Per the PWC-20, no evidence of a distinct withdrawal syndrome was observed during the 2 weeks following esketamine cessation.

Esketamine
Long-term Trials

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SUSTAIN-2[2]

Phase 3, Open-label, Multicenter, Long-term (up to 1 Year Exposure) Study

N=802

Key Inclusion Criteria[2]

Direct-entry
- Age ≥18 years
- DSM-5 diagnosis of MDD without psychotic features
- MADRS total score ≥22 at screening
- Nonresponse to ≥2 oral ADs (via the MGH-ATRQ)

Transfer-entry
- Completed double-blind induction phase of an acute study of elderly patients

Key Exclusion Critria[2]

- Homicidal or suicidal ideation
- Borderline, antisocial, histrionic, or narcissistic personality disorder
- Bipolar disorder or OCD
- Nonresponse to all 4 study ADs or esketamine or ketamine
- Clinically significant CVD or uncontrolled hypertension
- Substance or alcohol abuse

Study Design[2]

Direct-Entry Patients (n=691) | Transfer-Entry Nonresponders (n=88)

Transfer-Entry Responders (n=23)

Open-label Induction (4 Weeks) (n=779)

Open-label Optimization/ Maintenance (48 Weeks) (n=603)

Esketamine flexibly dosed, twice weekly (28, 56, or 84 mg based on age)
+
Oral AD (duloxetine, escitalopram, sertraline, or venlafaxine XR)
Transfer-entry patients continued same AD

Responders (n=580)

Esketamine
Transfer entry: 28 mg (week 5) →56 or 84 mg till week 8. Treatment reduced to weekly for 4 weeks, then weekly or every other week
+
Oral AD

Safety Endpoint[2]

TEAEs During the Induction + Optimization/Maintenance Phases

- **≥1 TEAE:** 90.1%
  - Most TEAEs were **mild or moderate** and **resolved** on the day of dosing
- TEAEs in ≥10% of patients:
  - Dizziness
  - Dissociation
  - Nausea
  - Headache
  - Somnolence
  - Dysgeusia
  - Hypoesthesia
  - Vertigo
  - Vomiting
  - Viral URTI
- **≥1 SAE:** 6.9%
- **TEAEs leading to discontinuation** of:
  - Esketamine: 9.5%
  - Oral AD: 4.1%
- **Deaths:** 2 (1 doubtfully related to esketamine)

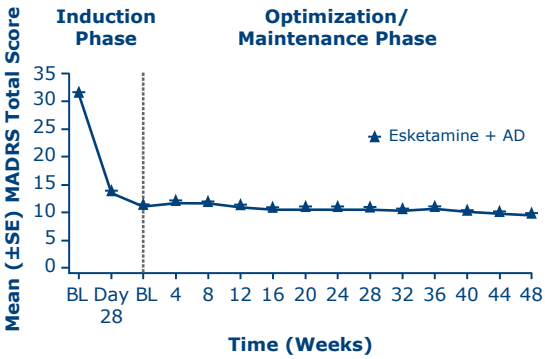
Other Safety Outcomes[2]

- Treatment-emergent **dissociative symptoms, sedation,** and **blood pressure increases** generally resolved by 1.5 hours postdose
- **Cognitive performance** either improved or remained stable through week 44
- There were no cases of **interstitial or ulcerative cystitis**
- New occurrences of **suicidal ideation**: 14.5%
- **Nasal tolerability** was acceptable

Efficacy Results[2]

- MADRS total score improved throughout the induction phase and was maintained through the optimization/maintenance phase

Mean MADRS Total Score Over Time



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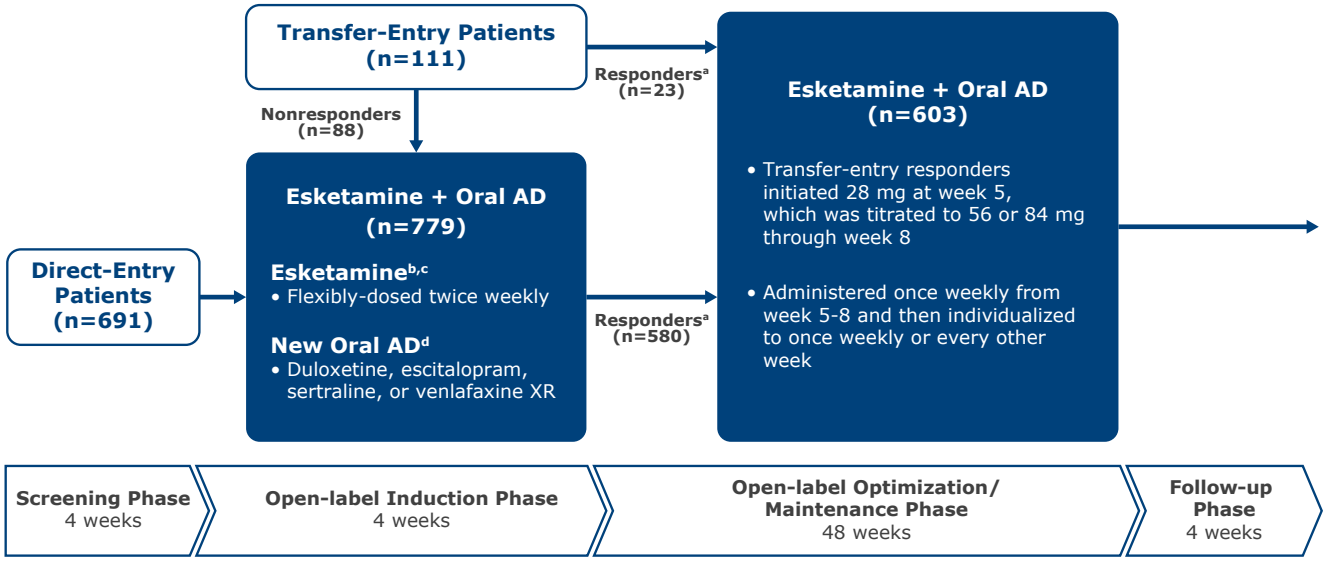
- SUSTAIN-2 (NCT02497287) was a phase 3, open-label, multicenter study conducted to evaluate the long-term (up to 1 year of exposure) safety, tolerability, and efficacy of esketamine nasal spray (28, 56, or 84 mg) plus a newly initiated oral AD in patients.[2]



[a]Response: ≥50% reduction in MADRS total score.

[b]Per protocol, esketamine was not recommended in patients <65 years old with a repeated blood pressure measurement >140/90 mm Hg or in patients ≥65 years old with a repeated blood pressure measurement >150/90 mm Hg. Esketamine was discontinued in patients <65 years old with blood pressure ≥200/120 mm Hg or in patients ≥65 years old with blood pressure ≥190/110 mm Hg.

[c]Dose adjusted based on clinician's judgment. Patients <65 years old received 56 mg esketamine followed by 56 or 84 mg; patients ≥65 years old received 28 mg esketamine followed by 28, 56, or 84 mg.

[d]Transfer-entry patients continued the same AD as in the acute trial.

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Inclusion Criteria[2]	Exclusion Criteria[2]
Direct-entry patients: • Age ≥18 years • DSM-5 diagnosis of MDD without psychotic features • MADRS total score of ≥22 at screening • Nonresponse to ≥2 ADs in the current episode of depression, assessed retrospectively via the MGH-ATRQ and medication records **Transfer-entry patients:** • Completed the double-blind induction phase of an acute study of elderly patients with TRD[6] • Aforementioned criteria for direct-entry patients	• History of prior nonresponse to all 4 oral ADs or esketamine or ketamine • Bipolar or related disorders; comorbid OCD; intellectual disability; autism spectrum disorder; or borderline, antisocial, histrionic, or narcissistic personality disorder • Homicidal or suicidal ideation with intent to act within 6 months prior to start of screening, per investigator's judgment or based on C-SSRS • History of moderate or severe substance or alcohol abuse (DSM-5 criteria) within 6 months before screening, except nicotine or caffeine • Clinically significant CVD or history of uncontrolled hypertension or hypertensive crisis

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Safety Endpoints[2]

- Assessment of TEAEs throughout the study
- Assessment of cognitive function at predose baseline and specified predose timepoints through computerized cognitive test battery (Cogstate) and HVLT-R
- Suicidal ideation and behavior measured with C-SSRS, dissociative symptoms scored with CADSS, psychotic and affective symptoms measured with the positive symptom subscale of BPRS+, and sedation using MOAA/S
- Bladder symptoms monitored using BPIC-SS
- Potential withdrawal symptoms assessed using PWC-20 (after induction and maintenance endpoints and at weeks 1, 2, and 4 of follow-up)
- Clinical laboratory tests, vital signs assessment, ECG, nasal examination, and nasal symptom questionnaire were evaluated at prespecified timepoints; respiratory and pulse oximetry monitored at each dosing session

Efficacy Endpoints[2]

- Change in MADRS total score from induction and maintenance baseline to endpoint
- Proportion of responders (≥50% reduction in MADRS total score) and remitters (MADRS total score ≤12)

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Characteristic[2]	**Enrolled Patients (n=802)**
Age, years, mean (SD)	52.2 (13.69)
Sex, female, n (%)	502 (62.6)
Race, white, n (%)	686 (85.5)
Nonresponse to 2 prior ADs, n (%)	465 (58.0)
History of suicidal ideation in past 6 months, n (%)	215 (26.9)
AD use,[a] n (%)	
Duloxetine	251 (31.3)
Escitalopram	237 (29.6)
Sertraline	157 (19.6)
Venlafaxine XR	156 (19.5)

[a]Number of evaluable patients, n=801.

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- **Median exposure** to esketamine was 22.9 weeks.[2]
- Most TEAEs were **mild or moderate** in intensity, occurred on dosing days, and **resolved** on the same day.[2]

TEAEs,[a] n (%)	4-Week Induction Phase (n=779)	48-Week Optimization/ Maintenance Phase (n=603)	Induction and Optimization/ Maintenance Phases (N=802)
Patients with ≥1 TEAE	653 (83.8)	516 (85.6)	723 (90.1)
Patients with ≥1 SAE	17 (2.2)	38 (6.3)	55 (6.9)[b]
TEAEs leading to esketamine discontinuation	53 (6.8)	23 (3.8)	76 (9.5)
TEAEs leading to oral AD discontinuation	20 (2.6)	14 (2.3)	33 (4.1)
Most Common TEAEs (≥10% of Patients in the Combined Phases Group)			
Dizziness	228 (29.3)	135 (22.4)	264 (32.9)
Dissociation	182 (23.1)	113 (18.7)	221 (27.6)
Nausea	157 (20.2)	84 (13.9)	201 (25.1)
Headache	137 (17.6)	114 (18.9)	200 (24.9)
Somnolence	94 (12.1)	85 (14.1)	134 (16.7)
Dysgeusia	77 (9.9)	54 (9.0)	95 (11.8)
Hypoesthesia	79 (10.1)	40 (6.6)	95 (11.8)
Vertigo	68 (8.7)	43 (7.1)	88 (11.0)
Vomiting	56 (7.2)	45 (7.5)	87 (10.8)
Viral URTI	19 (2.4)	70 (11.6)	82 (10.2)

[a]All enrolled analysis set (induction and optimization/maintenance phases combined): patients who received ≥1 dose of nasal spray study medication or oral AD.

[b]Five SAEs were considered esketamine-related by the investigator: anxiety and delusion (both in 1 patient), delirium (n=1), suicidal ideation (n=1), and suicidal attempt (n=1).

- There were 2 deaths: one considered by investigators to be doubtfully related to esketamine (60-year-old man who died due to acute cardiac and respiratory failure) and the other not considered by investigators to be related to esketamine (suicide-related death in a 55-year-old woman).[2]

Most Common TEAEs Leading to Discontinuation of Esketamine in ≥2 Patients

Most Common TEAEs[a] Leading to Discontinuation of Esketamine in ≥2 Patients[2]

TEAEs, n (%)	4-Week Induction Phase (n=779)	48-Week Optimization/ Maintenance Phase (n=603)	Induction and Optimization/ Maintenance Phases (N=802)
Anxiety	9 (1.2)	0	9 (1.1)
Suicidal ideation	3 (0.4)	4 (0.7)	7 (0.9)
Depression	3 (0.4)	3 (0.5)	6 (0.7)
Dizziness	6 (0.8)	0	6 (0.7)
Blood pressure increased	4 (0.5)	2 (0.3)	6 (0.7)
Dissociation	5 (0.6)	0	5 (0.6)
Muscular weakness	4 (0.5)	0	4 (0.5)
Vomiting	3 (0.4)	0	3 (0.4)
Hypertension	2 (0.3)	1 (0.2)	3 (0.4)
Suicide attempt	1 (0.1)	1 (0.2)	2 (0.2)
Headache	2 (0.3)	0	2 (0.2)
Sedation	2 (0.3)	0	2 (0.2)
Somnolence	2 (0.3)	0	2 (0.2)
Nausea	2 (0.3)	0	2 (0.2)
Vertigo	1 (0.1)	1 (0.2)	2 (0.2)

[a]TEAE that started in the optimization/maintenance phase and resulted in discontinuation in the follow-up phase is counted as treatment-emergent in the optimization/maintenance phase.

TEAE, treatment-emergent adverse event.

Most Common TEAEs Leading to Discontinuation of Esketamine in ≥2 Patients

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Cognitive Function[2]

- Group mean performance on all Cogstate and HVLT-R tests either improved or remained stable through week 44 for the entire study population.
- In patients ≥65 years of age, simple and choice reaction time slowed beginning at week 20 of the optimization/maintenance phase.
  - Among patients with reaction times at baseline that were within age-adjusted norms, 7 showed consistent slowing as the study progressed, and none had impaired reaction time at study endpoints and follow-up (z score <-1.5 on detection or identification tasks).

Dissociative Symptoms and Sedation[2]

- Dissociative and perceptual changes, as measured by CADSS, peaked at 40 minutes postdose and generally resolved by 1.5 hours. The magnitude of change attenuated with repeated dosing.
- Clinically-relevant sedation (MOAA/S score ≤3) occurred in 8.4% of patients in the induction phase and 7.0% of patients in the optimization/maintenance phase.
  - The longest period of sedation started at 45 minutes postdose and lasted for 1.5 hours.

Suicidal Ideation[2]

- New occurrences of suicidal ideation and behavior was reported in 114/784 patients (14.5%) using the C-SSRS assessment.
- A total of 8 patients reported suicidal behavior.

Withdrawal Symptoms[2]

- Withdrawal symptoms, measured by the mean (SD) PWC-20, was 7.9 (6.91) at week 1 of follow-up, 8.0 (7.42) at week 2, and 7.7 (7.07) at week 4.
- In patients who discontinued the optimization/maintenance phase (n=110), the most common "withdrawal" symptom was fatigue-lethargy/lack of energy (25.0%) at week 1 and insomnia (22.7%) at study end.

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Renal Disorders[2]

- There were no reported cases of interstitial or ulcerative cystitis.
- TEAEs related to renal and urinary system disorders were reported in 136 (17.0%) patients and UTIs were reported in 8.1% of patients. Most cases of urinary symptoms were mild to moderate and resolved within 2 weeks.
- Overall, 14 patients had multiple episodes of BPIC-SS scores >18 (UTI/cystitis, n=6; dysuria and pollakiuria, n=2; history of benign prostate hyperplasia, n=1; signs of UTI on urinalysis, n=3; and no AEs/laboratory changes, n=2).

Increases in Blood Pressure[2]

- Blood pressure increases were reported 40 minutes postdose and generally returned to near baseline values by 1.5 hours.
- Overall, 33 patients (4.1%) experienced systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg; 4 patients were withdrawn from the study due to increased blood pressure.

Nasal Symptoms[2]

- Nasal tolerability was considered acceptable (≥99% of patients had a normal nasal examination).
- Responses to the Nasal Symptom Questionnaire:

Nasal Symptoms, %	Induction	Optimization/Maintenance
Taste disturbance	10.2	11.0
Postnasal drip	9.9	11.0
Stuffy nose	5.9	9.1

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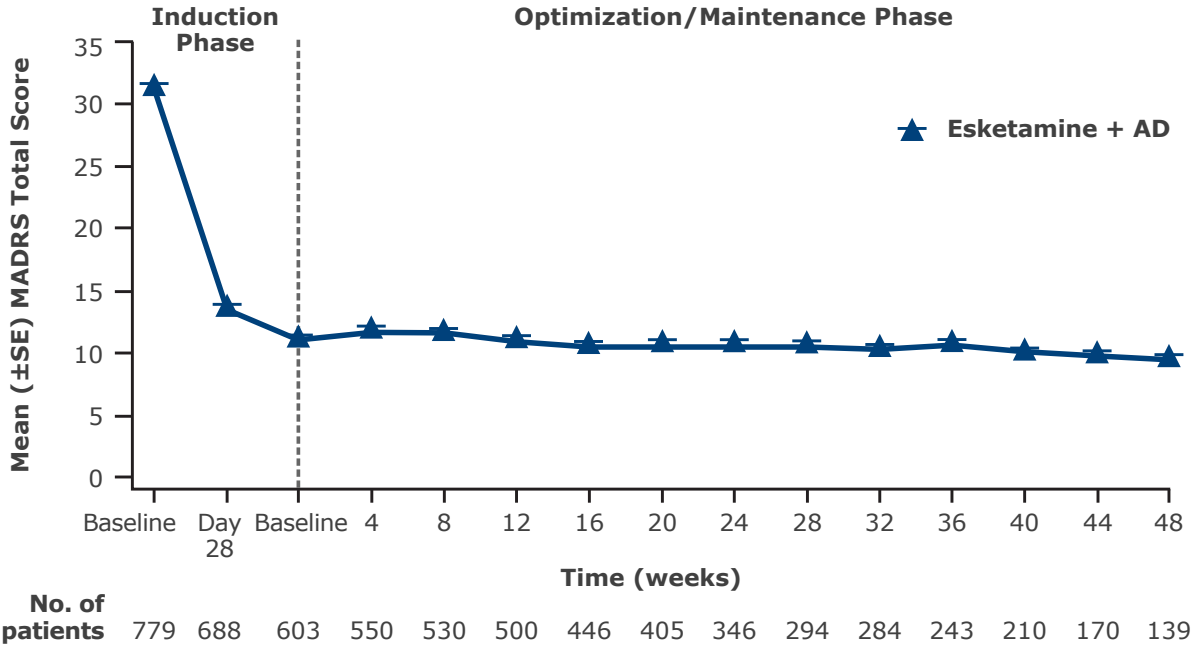
- **MADRS total score** improved throughout the induction phase (mean [SD] change: -16.4 [8.76]) and appeared to be maintained from optimization/maintenance baseline to optimization/maintenance endpoint (mean [SD] change: 0.3 [8.12]).[2]

Mean MADRS Total Score Over Time



Full analysis sets: All patients who received ≥1 dose of esketamine or AD in the open-label induction or optimization/maintenance phases.

Wajs E, Aluisio L, Holder R, et al. Esketamine nasal spray plus oral antidepressant in patients with treatment-resistant depression: assessment of long-term safety in a phase 3, open-label study (SUSTAIN-2). J *Clin Psychiatry.* 2020;81(3):19m12891. Copyright 2020. Physicians Postgraduate Press. Adapted by permission.

- The percentage of responders and remitters increased over time during the induction phase.[2]

Efficacy Response	Induction	Optimization/Maintenance
Responders,[a] n/N (%)	593/756 (78.4)	461/603 (76.5)
Remitters,[b] n/N (%)	357/756 (47.2)	351/603 (58.2)

[a]≥50% reduction in the MADRS total score.
[b]MADRS total score ≤12.

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AD	Antidepressant	**MGH-ATRQ**	Massachusetts General Hospital - Antidepressant Treatment Response Questionnaire
AE	Adverse event	**MINI**	Mini International Neuropsychiatric Interview
BL	Baseline	**MOAA/S**	Modified Observer's Assessment of Alertness/Sedation
BPIC-SS	Bladder Pain/Interstitial Cystitis Symptom Score	**NE**	Not estimable
BPRS+	Brief Psychiatric Rating Scale	**NNT**	Number needed to treat
CADSS	Clinician-Assessed Dissociative Symptom Scale	**OCD**	Obsessive compulsive disorder
CI	Confidence interval	**PWC-20**	Physician Withdrawal Checklist, 20-Item
C-SSRS	Columbia - Suicide Severity Rating Scale	**SAE**	Serious AE
CVD	Cardiovascular disease	**SD**	Standard deviation
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition	**SE**	Standard error
ECG	Electrocardiogram	**SNRI**	Serotonin-norepinephrine reuptake Inhibitor
ECT	Electroconvulsive therapy	**SSRI**	Selective serotonin reuptake Inhibitor
HR	Hazard ratio	**TEAE**	Treatment-emergent AE
HVLT-R	Hopkins Verbal Learning Test – Revised	**TRD**	Treatment-resistant depression
IDS-C_{30}	Inventory of Depressive Symptomatology-Clinician Rated —30-item	**URTI**	Upper respiratory tract infection
MADRS	Montgomery-Åsberg Depression Rating Scale	**UTI**	Urinary tract infection
MDD	Major depressive disorder	**XR**	Extended release

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A literature search of MEDLINE®, BIOSIS®, DERWENT®, and EMBASE® (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 11 May 2020.

Thank you for your interest in SPRAVATO® (esketamine). The information is presented in response to your unsolicited inquiry. This information is taken from the references cited, but is not intended to serve as a substitute for review of these references. This information is not intended to advocate the use of our product in any manner other than as described in the product monograph. Please refer to the SPRAVATO® Product Monograph available at http://www.janssen.com/canada/products for full prescribing information.

For any questions, please contact Janssen Medical Information at:
1.800.567.3331 or 1.800.387.8781 or http://www.janssenmedicalinformation.ca

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