

Data Supplement for Singh et al., A Double-Blind, Randomized, Placebo-Controlled, Dose-Frequency Study of Intravenous Ketamine in Patients With Treatment-Resistant Depression. Am J Psychiatry (doi: 10.1176/appi.ajp.2016.16010037)

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TABLE S1: MADRS total score – open-label and follow-up phase (OL ITT analysis set)

	MADRS total score		MADRS total score – change from baseline	
	Mean	SD	Mean	SD
OL Ketamine 2X/WK				
Day 4, (n = 12)	23.5	11.00	-12.2	12.81
FU Ketamine 2X/WK				
Day 4, (n = 10)	21.7	12.47	-12.6	12.25
Day 11, (n = 5)	11.4	9.13	-26.2	12.21
Day 18, (n = 2)	17.5	0.71	-19.0	0.0
OL Ketamine 3X/WK				
Day 3, (n = 15)	23.5	10.30	-13.3	9.62
Day 5, (n = 16)	22.6	12.11	-14.0	12.50
FU Ketamine 3X/WK				
Day 4, (n = 11)	22.4	13.68	-14.6	14.47
Day 11, (n = 7)	26.4	13.35	-13.4	12.00
Day 18, (n = 7)	28.7	13.26	-9.3	12.74
2X/Week = two-times weekly; 3X/Week = three-times weekly; FU = follow-up; ITT = intent-to-treat; MADRS = Montgomery-Asberg Depression Rating Scale; OL = open-label; SD = standard deviation.				

TABLE S2: Pharmacokinetic parameters of ketamine and norketamine

Treatment/Day		C _{max} (ng/mL)		t _{max} (h)			AUC _{6h} (h·ng/mL)		t _{1/2} (h)	
		Mean	SD	Median	Range		Mean	SD	Mean	SD
					Min	Max				
Ketamine										
2X/Week	Day 1 (n = 16)	207	83.0	0.67	0.63	0.83	312	67.9	2.18	0.43 ^a
	Day 15 (n = 14)	219	69.4	0.67	0.63	1.00	342	66.7	2.39	0.36 ^b
3X/Week	Day 1 (n = 16)	168	34.4	0.66	0.33	0.75	295	42.8 ^c	2.18	0.40 ^a
	Day 15 (n = 15)	189	74.4	0.67	0.5	0.83	293	65.6 ^d	2.21	0.36 ^c
Norketamine										
2X/Week	Day 1 (n = 16)	77.3	24.2	1.00	0.83	2.00	259	73.2	5.75	3.60
	Day 15 (n = 14)	76.2	19.8	1.00	0.83	3.00	265	76.9	5.96	2.66 ^a
3X/Week	Day 1 (n = 16)	63.5	20.4	1.00	0.83	2.00	232	70.3	6.70	2.54
	Day 15 (n = 15)	71.6	23.9	1.00	0.75	2.00	237	69.7	6.06	2.49
2X/Week = two-times weekly; 3X/Week = three-times weekly; min: minimum; max: maximum; ^a n = 13; ^b n = 9; ^c n = 15; ^d n = 14; ^e n = 8.										

TABLE S3: Changes in C-SSRS categories scores from baseline (safety analysis set)

Baseline Category	On Treatment Category		
	No Sui. Idea. or behavior	Suicidal ideation	Suicidal behavior
Placebo 2X/WK (n = 16)			
No Sui. Idea. or behavior	4	0	0
Suicidal ideation	1	2	0
Suicidal behavior	3	6	0
Ketamine 2X/WK (n = 18)			
No Sui. Idea. or behavior	8	0	0
Suicidal ideation	1	3	0
Suicidal behavior	5	1	0
Placebo 3X/WK (n = 16)			
No Sui. Idea. or behavior	3	0	0
Suicidal ideation	3	3	0
Suicidal behavior	2	5	0
Ketamine 3X/WK (n = 17)			
No Sui. Idea. or behavior	7	0	0
Suicidal ideation	4	2	0
Suicidal behavior	2	2	0
OL Ketamine 2X/WK (n = 13)			
No Sui. Idea. or behavior	2	0	0
Suicidal ideation	1	2	0
Suicidal behavior	6	2	0
OL Ketamine 3X/WK (n = 18)			
No Sui. Idea. or behavior	4	0	0
Suicidal ideation	3	3	0
Suicidal behavior	5	3	0
2X/Week = two-times weekly; 3X/Week = three-times weekly; C-SSRS=Columbia Suicide Severity Rating Scale; Idea. = ideation; OL = open-label; Sui. = suicidal			

FIGURE S1: MADRS total scores over time for individual patients (ITT [DB] analysis set): A). Ketamine 2X/Week Patients; B). Ketamine 3X/Week Patients

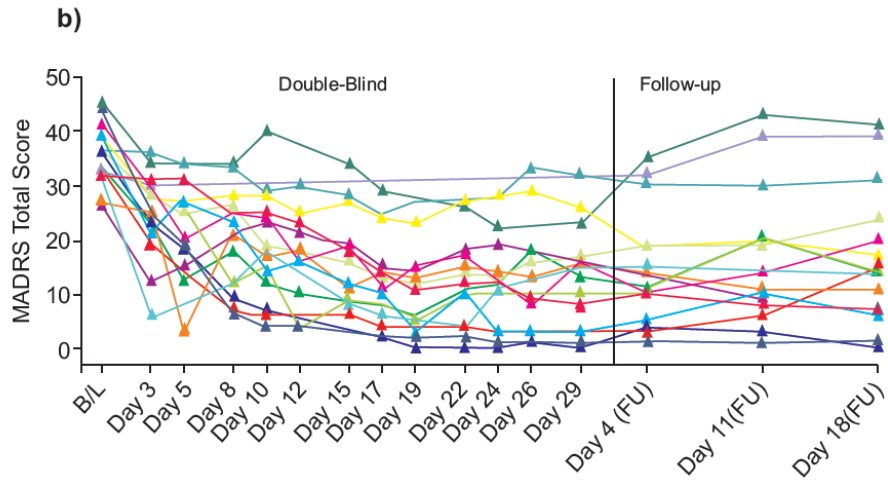
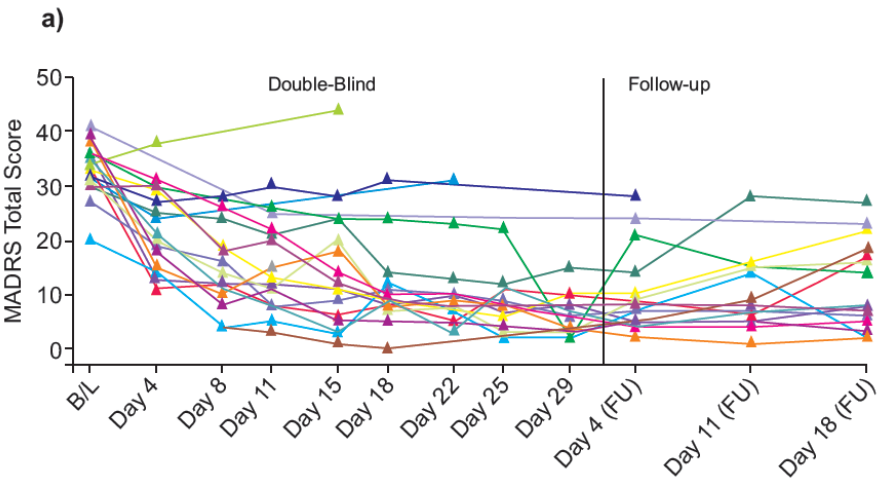


FIGURE S2: Ketamine and norketamine plasma concentration-time profiles

