Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

Supplement

eTable 1: Ketamine responders who remained much improved 2 weeks later

IES-R Total (Baseline)	IES-R Total (Week 1)	IES-R Total (Day 10)	IES-R Total (Week 2)	CAPS Total (Baseline)	CAPS Total (Week 1)	CAPS Total (Week 2)	CGI-I (Week 1)	CGI-I (Week 2)
60	18	25.14	26	97	54	44	2	.
54	17	28	28	83	22	45	2	.
24	3	3	2	60	13	11	2	2
15	1	4	6	52	16	11	2	2
19	8.38	3	1	71	45	25	.	.
59	10	15	14	93	41	28	2	2
17	2	3	0	73	33	19	3	3

Midazolam responder who remained much improved 1 week later:

43	12.57	6	5	62	50	30	4	4

Note: For this study, the IES-R was modified to inquire about symptoms over the previous 24 hours (instead of previous 7 days).

About the unmodified IES-R: “There are no "cut-off" points for the IES-R, nor are they envisioned or appropriate, despite analyses that present them… The IES-R is intended to give an assessment of symptomatic status over the last 7 days with respect to the 3 domains of PTSD symptoms stemming from exposure to a traumatic stressor.” (in http://www.berkshirehealthsystems.org/workfiles/psych/Impact%20of%20event%20scale%20IES%20R.pdf, authored by Weiss, D.S.)

eTable 2: Baseline, Week-1 and Week-2 IES-R, CAPS, and CGI-I scores, full sample

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
IES-R_baseline	IES-R Total (Baseline)	35	48.44	16.61	15	74
CAPS_baseline	CAPS Total (Baseline)	35	80.09	12.36	52	100
CGII_day7	CGI-I (Week 1)	33	3.489	0.97	2	5
IES-R_day7	IES-R Total (Week 1)	34	30.42	17.71	1	63
CAPS_day7	CAPS Total (Week 1)	35	59.34	21.18	13	94
CGII_day13	CGI-I (Week 2)	24	3.50	0.88	2	5
IES-R_day13	IES-R Total (Week 2)	32	28.66	16.32	0	61
CAPS_day13	CAPS Total (Week 2)	35	62.89	24.86	11	103

Note: IES-R = Impact of Event Scale – Revised; CAPS = Clinician-Administered PTSD Scale; CGI-I = Clinical Global Impression – Improvement (the CGI-I is not administered at baseline); Std Dev = standard deviation.

By group:

eTable 3: Baseline, Week-1 and Week-2 IES-R, CAPS, and CGI-I scores, by treatment group

Randomization sequence = 1 (Ketamine first)

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
IES-R_baseline	IES-R Total (Baseline)	19	44.84	20.13	15	74
CAPS_baseline	CAPS Total (Baseline)	19	81.42	13.96	52	100
CGII_day7	CGI-I (Week 1)	18	3.22	1.06	2	5
IES-R_day7	IES-R Total (Week 1)	19	25.76	19.40	1	63
CAPS_day7	CAPS Total (Week 1)	19	54.00	23.63	13	90
CGII_day13	CGI-I (Week 2)	13	3.15	0.80	2	4
IES-R_day13	IES-R Total (Week 2)	18	25.67	17.77	0	61
CAPS_day13	CAPS Total (Week 2)	19	56.21	28.43	11	103

Note: IES-R = Impact of Event Scale – Revised; CAPS = Clinician-Administered PTSD Scale; CGI-I = Clinical Global Impression – Improvement (the CGI-I is not administered at baseline); Std Dev = standard deviation

Randomization sequence = 2 (Midazolam first)

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
IES_baseline	IES-R Total (Baseline)	16	52.70	10.16	32	72
CAPS_baseline	CAPS Total (Baseline)	16	78.50	10.36	57	95
CGII_day7	CGI-I (Week 1)	15	3.80	0.77	2	5
IES_day7	IES-R Total (Week 1)	15	36.32	13.73	11	53
CAPS_day7	CAPS Total (Week 1)	16	65.69	16.36	31	94
CGII_day13	CGI-I (Week 2)	11	3.91	0.83	2	5
IES_day13	IES-R Total (Week 2)	14	32.51	13.92	5	51
CAPS_day13	CAPS Total (Week 2)	16	70.81	17.55	30	99

Note: IES-R = Impact of Event Scale – Revised; CAPS = Clinician-Administered PTSD Scale; CGI-I = Clinical Global Impression – Improvement (the CGI-I is not administered at baseline); Std Dev = standard deviation.

eTable 4: Frequency table for response[a] by treatment

Table of IES-R_response by randomization sequence			
IES-R_response	**Randomization sequence**		
Frequency **Percent** **Row Pct** **Col Pct**	**Ketamine first**	**Midazolam first**	**Total**
No	9 25.71 45.00 47.37	11 31.43 55.00 68.75	20 57.14
Yes	10 28.57 66.67 52.63	5 14.29 33.33 31.25	15 42.86
Total	19 54.29	16 45.71	35 100.00

[a] Response = 50% improvement in IES-R score at 24 hours post-infusion; 52.63% responded after ketamine infusion and 31.25% responded after midazolam infusion.

eTable 5: Adverse Events in Patients During Ketamine Infusion (N=38) and Midazolam Infusion (N=31)

	Infusion Day [b]				24 Hours Post-Infusion			
	New Onset or Worsening		Distressing [c]		New Onset or Worsening		Distressing [c]	
Adverse Event [a]	Ketamine N (%)	Midazolam N (%)	Ketamine N (%)	Midazolam N (%)	Ketamine N (%)	Midazolam N (%)	Ketamine N (%)	Midazolam N (%)
Gastrointestinal			5 (13.16)	1 (3.23)			2 (5.26)	1 (3.23)
Diarrhea	0	0			3 (7.89)	2 (6.45)		
Constipation	0	0			0	0		
Dry mouth	9 (23.68)	2 (6.45)			1 (2.63)	2 (6.45)		
Nausea/vomiting	8 (21.05)	0			2 (5.26)	0		
Heart			5 (13.16)	0			1 (2.63)	0
Palpitation	2 (5.26)	0			1 (2.63)	0		
Dizziness on standing	6 (15.79)	2 (6.45)			0	3 (9.68)		
Chest pain	2 (5.26)	1 (3.23)			0	2 (6.45)		
Skin			1 (2.63)	2 (6.45)			2 (5.26)	3 (9.68)
Rash	0	0			1 (3.23)	0		
Increased perspiration	2 (5.26)	1 (3.23)			1 (3.23)	0		
Itching	0	0			1 (3.23)	0		
Dry skin	0	1 (3.23)			2 (6.45)	0		
Nervous system			7 (18.42)	1 (3.23)			1 (2.63)	1 (3.23)
Headache	6 (15.79)	2 (6.45)			2 (5.26)	2 (6.45)		
Tremors	0	1 (3.23)			0	0		
Poor coordination	6 (15.79)	1 (3.23)			1 (2.63)	0		
Dizziness	14 (36.84)	5 (16.13)			0	4 (12.90)		
Eyes/ears			5 (13.16)	1 (3.23)			1 (2.63)	1 (3.23)
Blurred vision	14 (36.84)	6 (19.35)			1 (2.63)	0		
Ringing in ears	3 (7.89)	0			2 (5.26)	1 (3.23)		
Genital/urinary			0	1 (3.23)			0	2 (6.45)
Difficulty urinating	0	2 (6.45)			0	1 (3.23)		
Painful urination	2 (5.26)	1 (3.23)			0	0		
Frequent urination	0	1 (3.23)			2 (5.26)	3 (9.68)		
Menstrual irregularity	0	0			0	0		
Sleep			5 (13.16)	7 (22.58)			5 (13.16)	6 (19.35)
Difficulty sleeping	N/A	N/A			3 (7.89)	3 (9.68)		
Sleeping too much	N/A	N/A			2 (5.26)	1 (3.23)		
Other			13 (34.21)	11 (35.49)			5 (13.16)	6 (19.35)
Anxiety	3 (7.89)	1 (3.23)			2 (5.26)	0		
Poor concentration	4 (10.53)	5 (16.13)			0	1 (3.23)		
General malaise	3 (7.89)	1 (3.23)			0	0		
Restlessness	8 (21.05)	1 (3.23)			5 (13.16)	3 (9.68)		
Fatigue	9 (23.68)	5 (16.13)			1 (2.63)	1 (3.23)		
Decreased energy	6 (15.79)	3 (9.68)			0	0		

Note: [a] From the modified version of the Patient Rated Inventory of Side Effects (PRISE), excluding sexual functioning category, and sleep category on infusion days. [b] Measured at 40 minutes, 120 minutes, and 240 minutes post-infusion. [c] N (%) of patients who found at least one side effect distressing in that category (e.g., gastrointestinal).