Supplementary Material

Article Title: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial of *S*-Adenosyl-L-Methionine (SAMe) Versus Escitalopram in Major Depressive Disorder

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1.   **eTable 1**   Time course of Main Outcome Instruments for Intent-to-Treat Sample (N=189)

Disclaimer

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Supplementary eTable 1: Time course of Main Outcome Instruments for Intent-to-Treat Sample (N = 189)

Group	Baseline		Week 1		Week 2		Week 4		Week 6		Week 8		Week 10		Week 12	
HAM-D-17	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
PBO	19.43	4.07	16.71	5.06	15.37	5.19	14.42	5.67	13.32	5.66	13.08	5.95	12.17	6.93	12.00	6.96
SAMe	18.98	5.09	16.27	6.29	13.83	6.14	11.91	7.25	11.09	7.22	9.68	6.87	8.85	5.85	11.12	6.74
ESC	19.25	4.88	17.51	5.47	15.81	5.70	14.43	6.16	13.23	7.00	11.86	7.08	12.18	8.14	10.77	6.58
IDS-SR																
PBO	37.44	11.56	32.78	11.34	31.45	11.59	28.23	11.66	27.88	12.60	28.89	12.60	26.41	14.22	24.17	13.58
SAMe	34.87	9.74	29.26	10.15	25.14	11.13	22.77	12.59	22.14	13.23	19.99	12.31	18.30	10.58	18.83	10.90
ESC	37.54	12.35	32.47	12.89	31.32	14.21	29.94	14.01	25.80	13.59	25.78	16.21	25.18	16.75	24.72	16.00
CGI-S																
PBO	4.29	0.65	3.96	0.89	3.63	0.85	3.38	1.19	3.17	1.20	3.14	1.29	3.00	1.37	2.93	1.51
SAMe	4.38	0.76	3.84	1.23	3.42	1.23	3.09	1.41	2.78	1.46	2.73	1.39	2.31	1.21	2.65	1.39
ESC	4.44	0.69	3.90	0.91	3.66	0.89	3.46	1.21	3.19	1.26	2.83	1.27	2.84	1.35	2.61	1.42
CGI-I																
PBO	3.91	0.48	3.48	0.75	3.30	0.73	2.83	0.96	2.76	0.99	2.94	1.15	2.74	1.21	2.53	1.36
SAMe	3.90	0.63	3.36	0.80	3.14	1.00	2.84	1.29	2.62	1.25	2.30	1.15	2.11	1.08	2.41	1.18
ESC	3.97	0.26	3.42	0.85	3.11	0.78	2.95	1.02	2.73	1.05	2.43	1.07	2.53	1.16	2.39	1.29

HAMD-17: 17-item Hamilton Depression Rating Scale

IDS-SR: Inventory of Depressive Symptomatology – Self-Rated

CGI-S: Clinical Global Improvement Scale - Severity

CGI-I: Clinical Global Improvement Scale – Improvement

SAMe: S-Adenosyl methionine

ESC: Escitalopram

PBO: Placebo

SAMe vs ESC: No significant difference in HAM-D-17 score was found at any time point, but trends were seen at Week 4 (p=0.083) and Week 10 (p=0.055). Significant difference in IDS-SR was seen at Week 2 (p= 0.019), Week 4 (p=0.013), and Week 10 (p=0.047). No significant difference in CGI-S was seen at any time point, but a trend was seen at Week 10 (p=0.094).

ESC vs PBO: No significant differences were seen in HAM-D-17, IDS-SR, or CGI-S at any time point. A trend was seen for CGI-I at Week 8 (p= 0.054).

SAMe vs PBO: Significant differences in HAM-D-17 scores were seen at Week 8 (p=0.026) and Week 10 (p=0.034). Significant differences in IDS-SR were seen at Week 4 (p=0.033), Week 6 (p=0.044), Week 8 (p=0.003), and Week 10 (p=0.010). Significant differences were seen for CGI-S at Week 10 (p=0.031), and for CGI-I at Week 8 (p=0.019) and Week 10 (p=0.028).