

Supplementary TOC

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Supplementary Table 1. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 based on treatment assignment

Variable, median (IQR)	Sertraline N=97			Placebo N=96			Between-Groups <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	13.0 (12.0, 15.0)	9.0 (6.0, 13.0)*	-4.0 (-7.0, -1.0)	14.0 (12.0, 16.0)	10.0 (7.0, 12.0)*	-4.0 (-7.0, -2.0)	0.76	0.99	0.83
Albumin, g/dL	3.8 (3.4, 4.1)	3.9 (3.5, 4.1)	0.0 (-0.3, 0.1)	3.9 (3.6, 4.3)	3.9 (3.5, 4.2)	-0.05 (-0.2, 0.2)	0.07	0.40	0.98
Pre-albumin, mg/dL	31.0 (26.0, 35.0)	29.0 (26.0, 35.0)	0.0 (-5.0, 3.0)	29.5 (25.0, 35.0)	30.0 (26.0, 38.0)	0.0 (-3.0, 4.0)	0.26	0.67	0.20
IL-6, pg/mL	3.9 (2.3, 7.8)	3.7 (2.3, 5.7)	0.3 (-0.9, 1.6)	3.8 (2.3, 6.8)	4.0 (2.9, 6.1)	0.2 (-0.8, 1.3)	0.84	0.26	0.93
hsCRP, mg/L	3.0 (1.1, 7.6)	3.0 (1.3, 8.8)	0.2 (-0.8, 1.9)	3.3 (1.5, 10.0)	3.9 (2.0, 7.8)	0.3 (-0.8, 2.7)	0.28	0.34	0.81

**P*<0.05 study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity C-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 2. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 based on treatment improvement (3-point decrease in QIDS-C₁₆)

Variable, median (IQR)	All Participants Improvers N=115			All Participants Non-Improvers N=47			Between-Groups <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	14.0 (12.0, 16.0)	7.0 (6.0, 10.0)*	-6.0 (-8.0, -4.0)	13.0 (12.0, 15.0)	14.0 (12.0, 16.0)	0.0 (-1.0, 2.0)	0.10	<0.001	<0.001
Albumin, g/dL	3.9 (3.5, 4.2)	3.9 (3.5, 4.1)	0.0 (-0.20, 0.10)	3.9 (3.5, 4.2)	4.0 (3.6, 4.2)	-0.1 (-0.3, 0.2)	0.83	0.37	0.87
Pre-albumin, mg/dL	30.0 (26.0, 34.0)	29.0 (26.0, 35.0)	0.0 (-3.0, 3.0)	33.5 (27.0, 41.0)	33.0 (25.0, 43.0)	0.0 (-4.5, 4.0)	0.01	0.14	0.84
IL-6, pg/mL	4.0 (2.5, 6.8)	3.8 (2.8, 5.6)	0.2 (-0.7, 1.3)	3.6 (2.0, 7.5)	4.4 (2.3, 7.1)	0.3 (-0.9, 2.1)	0.47	0.67	0.97
hsCRP, mg/L	4.6 (1.4, 9.1)	3.1 (1.8, 6.5)	0.1 (-1.1, 1.7)	2.4 (1.0, 6.2)	5.4 (1.3, 11.6)*	0.5 (-0.3, 6.2)	0.04	0.34	0.10

**P*<0.05 study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity C-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 3. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 based on treatment improvement (3-point decrease in QIDS-C₁₆) in the sertraline group

Variable, median (IQR)	Sertraline Improvers N=62			Sertraline Non-Improvers N=35			Between-Groups P Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	14.0 (12.0, 16.0)	7.0 (6.0, 9.0)	-7.0 (-9.0, -4.0)*	13.0 (12.0, 15.0)	15.0 (12.0, 16.0)	0.0 (-1.0, 3.0)	0.04	<0.001	<0.001
Albumin, g/dL	3.8 (3.5, 4.1)	3.8 (3.5, 4.1)	0.0 (-0.2, 0.1)	3.8 (3.3, 4.1)	3.9 (3.4, 4.2)	-0.2 (-0.3, 0.2)	0.40	0.73	0.64
Pre-albumin, mg/dL	30.5 (26.0, 34.0)	29.0 (26.0, 34.0)	0.0 (-5.0, 3.0)	34.0 (27.0, 42.0)	34.0 (25.0, 43.0)	1.0 (-5.0, 3.0)	0.048	0.24	0.73
IL-6, pg/mL	4.0 (2.5, 8.0)	3.7 (2.7, 5.6)	0.0 (-1.2, 1.5)	3.5 (1.8, 7.5)	3.6 (2.3, 7.7)	0.5 (-0.8, 2.8)	0.22	0.74	0.30
hsCRP, mg/L	5.0 (1.7, 8.6)	3.0 (1.8, 6.7)	0.1 (-1.3, 1.8)	1.4 (0.6, 3.6)	2.9 (1.0, 10.8)	0.4 (-0.3, 2.1)	0.005	0.78	0.27

* $P < 0.05$ study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity C-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 4. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 on treatment improvement (3-point decrease in QIDS-C₁₆) in the placebo group

Variable, median (IQR)	Placebo Improvers N=69			Placebo Non-Improvers N=27			Between-Groups <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	14.0 (12.0, 16.0)	8.0 (6.0, 10.0)*	-6.0 (-8.0, -4.0)	14.0 (12.0, 15.0)	14.0 (12.0, 16.0)	0.0 (-1.0, 1.0)	0.86	<0.001	<0.001
Albumin, g/dL	3.9 (3.5, 4.2)	3.9 (3.5, 4.1)	-0.1 (-0.2, 0.2)	4.1 (3.7, 4.3)	4.0 (3.6, 4.2)	0.0 (-0.1, 0.1)	0.15	0.30	0.42
Pre-albumin, mg/dL	29.0 (25.0, 34.0)	30.0 (26.0, 35.0)	0.5 (-3.0, 4.0)	32.0 (27.0, 39.0)	31.0 (26.5, 40.5)	0.0 (-0.4, 8.0)	0.13	0.37	0.99
IL-6, pg/mL	3.9 (2.3, 6.4)	3.9 (2.9, 5.4)	0.3 (-0.3, 1.2)	3.8 (2.5, 8.1)	5.4 (2.9, 7.1)	-0.1 (-1.5, 1.8)	0.72	0.36	0.34
hsCRP, mg/L	3.9 (1.2, 9.6)	3.5 (1.8, 6.5)	0.2 (-0.8, 1.6)	3.1 (1.7, 12.4)	7.6 (2.4, 11.6)	1.0 (-0.9, 6.8)	0.94	0.06	0.25

**P*<0.05 study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity c-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 5. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 on treatment improvement (3-point decrease in QIDS-C₁₆)

Variable	Treatment group x improvement status interaction <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	0.21	0.26	0.14
Albumin, g/dL	0.01	0.60	0.39
Pre-albumin, mg/dL	0.90	0.84	0.82
IL-6, pg/mL	0.28	0.44	0.15
hsCRP, mg/L	0.04	0.19	0.86

Abbreviations: hsCRP, high sensitivity C-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 6. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 based on treatment response ($\geq 50\%$ decrease in QIDS-C₁₆)

Variable, median (IQR)	All Participants Responders N=55			All Participants Non-Responders N=138			Between-Groups P Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	14.0 (12.0, 16.0)	5.0 (4.0, 6.0)*	-8.0 (-10.0, -7.0)	13.5 (12.0, 16.0)	11.0 (9.0, 14.0)*	-3.0 (-5.0, 0.0)	0.88	<0.001	<0.001
Albumin, g/dL	3.8 (3.5, 4.2)	3.9 (3.5, 4.1)	0.0 (-0.2, 0.2)	3.0 (3.5, 4.2)	3.9 (3.5, 4.2)	0.0 (-0.2, 0.1)	0.49	0.67	0.51
Pre-albumin, mg/dL	30.0 (25.0, 34.0)	30.0 (27.0, 35.0)	0.0 (-2.0, 3.0)	31.0 (27.0, 35.0)	29.0 (26.0, 37.0)	0.0 (-4.0, 3.0)	0.21	0.56	0.67
IL-6, pg/mL	3.9 (2.3, 6.8)	3.6 (2.6, 4.7)	0.1 (-1.0, 1.1)	3.8 (2.3, 7.1)	4.0 (2.8, 6.4)	0.3 (-0.8, 1.8)	0.95	0.21	0.42
hsCRP, mg/L	4.4 (1.9, 13.8)	3.3 (2.0, 4.7)	-0.02 (-2.1, 1.0)	3.1 (1.1, 7.5)	3.7 (1.7, 8.8)*	0.4 (-0.5, 3.3)	0.18	0.44	0.03

* $P < 0.05$ study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity c-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 7. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 based on treatment response ($\geq 50\%$ decrease in QIDS-C₁₆) in the sertraline group

Variable, median (IQR)	Sertraline Responders N=31			Sertraline Non-Responders N=66			Between-Groups <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	15.0 (12.0, 17.0)	6.0 (4.0, 6.0)*	-9.0 (-11.0, -7.0)	13.0 (12.0, 15.0)	12.0 (9.0, 15.0)*	-2.0 (-4.0, 0.0)	0.08	<0.001	<0.001
Albumin, g/dL	3.8 (3.5, 4.1)	3.9 (3.5, 4.1)	0.0 (-0.2, 0.4)	3.8 (3.4, 4.1)	3.9 (3.5, 4.1)	-0.1 (-0.3, 0.1)	0.94	0.85	0.52
Pre-albumin, mg/dL	31.0 (26.0, 34.0)	30.0 (27.0, 33.0)	-1.0 (-2.0, 3.0)	32.0 (27.0, 38.0)	29.0 (25.0, 37.0)	0.0 (-5.0, 3.0)	0.26	0.93	0.91
IL-6, pg/mL	3.9 (2.5, 7.0)	3.6 (2.5, 4.4)	0.2 (-0.7, 1.1)	3.7 (2.1, 8.0)	4.0 (2.3, 6.5)	0.3 (-0.9, 3.5)	0.47	0.44	0.45
hsCRP, mg/L	5.0 (2.0, 14.6)	3.2 (2.0, 5.2)	0.3 (-1.7, 1.8)	2.7 (0.8, 6.0)	2.8 (1.2, 9.2)	0.2 (-0.5, 2.1)	0.03	0.62	0.72

* $P < 0.05$ study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity c-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 8. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 based on treatment response ($\geq 50\%$ decrease in QIDS-C₁₆) in the placebo group

Variable, median (IQR)	Placebo responders N=24			Placebo non-responders N=72			Between-Groups <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	13.0 (11.5, 15.0)	5.0 (4.5, 6.0)*	-8.0 (-9.0, -7.0)	14.0 (12.0, 16.0)	11.0 (9.0, 13.5)*	-3.0 (-5.0, -1.0)	0.10	<0.001	<0.001
Albumin, g/dL	3.8 (3.5, 4.2)	4.0 (3.5, 4.2)	-0.1 (-0.2, 0.2)	4.0 (3.6, 4.3)	3.9 (3.6, 4.2)	0.0 (-0.2, 0.1)	0.34	0.81	0.82
Pre-albumin, mg/dL	27.0 (24.0, 34.5)	34.5 (25.0, 38.5)	1.0 (-2.5, 5.0)	30.0 (27.0, 35.0)	30.0 (26.0, 35.0)	0.0 (-3.0, 3.0)	0.41	0.44	0.50
IL-6, pg/mL	3.0 (2.2, 6.8)	3.6 (2.6, 5.2)	0.1 (-1.5, 1.4)	4.1 (2.5, 6.7)	4.1 (2.9, 6.2)	0.3 (-0.4, 1.2)	0.45	0.51	0.70
hsCRP, mg/L	3.2 (1.3, 9.1)	3.4 (2.0, 4.5)	-0.4 (-9.3, 0.2)	3.7 (1.7, 10.0)	4.9 (1.8, 8.8)*	0.8 (-0.1, 3.9)	0.80	0.13	0.008

* $P < 0.05$ study exit value versus baseline value within-group

Abbreviations: hsCRP, high sensitivity c-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale

Supplementary Table 9. Inflammatory markers and total QIDS-C₁₆ scores at baseline and week 12 on treatment response ($\geq 50\%$ decrease in QIDS-C₁₆)

Variable	Treatment group x response status interaction <i>P</i> Values		
	Baseline	Study Exit	Baseline to Study Exit
QIDS-C ₁₆	0.02	0.62	0.04
Albumin, g/dL	0.48	0.95	0.70
Pre-albumin, mg/dL	0.84	0.57	0.73
IL-6, pg/mL	0.30	0.94	0.82
hsCRP, mg/L	0.09	0.22	0.08

Abbreviations: hsCRP, high sensitivity C-reactive protein; IL-6, interleukin 6; QIDS-C₁₆, 16-item Quick Inventory of Depressive Symptomatology Clinician Rated scale