Supplementary material for Souery D. et al. What to expect from a third step in treatment resistant depression: A prospective open study on escitalopram, The World Journal of Biological Psychiatry, 2014, doi: 10.3109/15622975.2014.987814

Supplementary Table I. Socio-demographic and clinical features of the Intent To Treat patients (n = 417) at baseline.

Socio-demographic and clinical features	Intent To Treat MDD patients n = 417 Mean $\pm$ SD/n(%)
Age (years, n = 416)	47.29 $\pm$ 12.51
Males	140 (33.57)
Caucasians	386 (92.57)
Education	
Below Compulsory	58 (13.91)
Compulsory Education	125 (29.98)
Secondary School	142 (34.05)
University	92 (22.06)
Marital Status	
Single	97 (23.26)
Married/Cohabiting	209 (50.12)
Separated/Divorced	98 (23.50)
Widowed	13 (3.12)
Occupation	
Employee	236 (56.59)
Unemployed	98 (23.50)
Student/Retired	60 (14.39)
Unknown/Others	23 (5.52)
Outpatients (n = 413)	337 (81.60)
Onset (years, n = 334)	33.22 $\pm$ 13.16
Severity current episode (n = 403)	
Moderate	182 (45.16)
Severe without psychotic features	216 (53.60)
Severe with psychotic features	5 (1.24)
Duration current episode (days, n = 375)	169.00 $\pm$ 194.16
Number of lifetime episodes (n = 310)	
Range 1–10	3.04 $\pm$ 2.22
> 10	27 (8.01)
Duration hospitalization (weeks, n = 84)	13.80 $\pm$ 21.02
Age first hospitalization (n = 74)	38.30 $\pm$ 13.50
Melancholia (n = 414)	231 (55.80)
Major depressive episode features (n = 413)	
With full inter-episode recovery	71 (17.19)
Without full inter-episode recovery	52 (12.59)
Seasonal pattern	15 (3.63)
Atypical features	24 (5.81)
Catatonic features	12 (2.91)
Post partum onset	2 (0.48)
No features	237 (57.39)
Dysthymia (n = 414)	3 (0.72)
Suicide risk	230 (55.16)
Suicide risk level (n = 230)	
Low	115 (50.00)
Moderate	69 (30.00)
High	46 (20.00)
Current anxiety disorder	97 (23.26)
Current panic disorder	34 (8.15)
Current social phobia	26 (6.23)
Current obsessive compulsive disorder	12 (2.88)
Current post traumatic stress disorder	8 (1.92)
Generalized anxiety disorder	56 (13.43)
Current alcohol dependence	3 (0.72)

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Supplementary Table 1. (Continued)

Socio-demographic and clinical features	Intent To Treat MDD patients n = 417 Mean± SD/n(%)
Current alcohol abuse	2 (0.48)
Current substance dependence	2 (0.48)
Current substance abuse	0 (0.00)
Current anorexia nervosa	1 (0.24)
Current bulimia nervosa	3 (0.72)
Psychiatric antecedents (n = 415)	
Unipolar depressive disorder in 1st degree relatives	207 (49.88)
Unknown	31 (7.47)
Unipolar depressive disorder in 2nd degree relatives	69 (16.63)
Unknown	111 (26.75)
Bipolar disorder in 1st degree relatives	17 (4.10)
Unknown	50 (12.05)
Bipolar disorder in 2nd degree relatives	2 (0.48)
Unknown	102 (24.58)
Antecedents affected by any other psychiatric disorder	146 (35.18)
Unknown	49 (11.81)
Suicide or suicidal attempt in 1st and 2nd degree relatives	73 (17.51)
Unknown	61 (14.63)
Suicide in 1st and 2nd degree relatives	42 (10.12)
Unknown	43 (10.36)
Suicidal attempt(s) in 1st and 2nd degree relatives	48 (11.57)
Unknown	60 (14.46)
Sheehan Disability Scale (n = 415)	
Work	6.55 ± 2.48
Social life	6.80 ± 1.92
Family life/home responsibilities	6.29 ± 1.99

Supplementary Table II. Antidepressant treatments at inclusion of the Intent To Treat patients (n = 378; n = 39 were missing).

Antidepressant treatments at inclusion	Intent To Treat MDD patients n = 378 n(%)
Paroxetine	76 (20.11)
Sertraline	62 (16.40)
Citalopram	40 (10.58)
Fluoxetine	40 (10.58)
Fluvoxamine	19 (5.03)
Mirtazapine	33 (8.73)
Amytriptyline	3 (0.79)
Clomipramine	11 (2.91)
Imipramine	2 (0.53)
Nortriptyline	5 (1.32)
Trimipramine	2 (0.53)
Maprotiline	2 (0.53)
Dosulepine	3 (0.79)
Reboxetine	2 (0.53)
Trazodone	7 (1.85)
Bupropion	4 (1.06)
Mianserine	7 (1.85)
Others	60 (15.87)
Number of previous antidepressants prescribed for current or past episode (n = 270)	1.39 ± 1.28
Number of adequate* previous antidepressants prescribed for current or past episode (n = 165)	1.35 ± 0.89

*Duration of at least 4 weeks and a score ≥ 2 at the Modified Antidepressant Treatment History Form (ATHF).

Supplementary Table III. Main outcome measures of Completers in the two phases of the trial (n = 334 and n = 157, respectively).

Clinical features	Completers Venlafaxine Phase (n = 334) Mean $\pm$ SD/n(%)	Completers Escitalopram Phase (n = 157) Mean $\pm$ SD/n(%)
Response		
Responders	151 (45.21)	71 (45.22) (MADRS $\geq$ 50%) 86 (54.78) (MADRS > 25%)
Non responders	183 (54.79)	86 (54.78) (MADRS $\geq$ 50%) 71 (45.22) (MADRS > 25%)
Remission		
Remitters	83 (24.85)	39 (24.84)
Non remitters	251 (75.15)	118 (75.16)
Doses		
Day 0 – baseline	75.00 $\pm$ 0.00	
Day 14 (n = 406)	122.84 $\pm$ 37.96	
Day 28 (n = 366)	166.60 $\pm$ 42.11	
Day 42 – end of the venlafaxine phase (n = 318)	186.79 $\pm$ 43.67	
Day 42 – baseline of the escitalopram phase (n = 170)		10.00 $\pm$ 0.00
Day 56 (n = 169)		22.19 $\pm$ 4.15
Day 70 (n = 163)		25.15 $\pm$ 5.01
Day 84 – end of the escitalopram phase (n = 157)		26.43 $\pm$ 4.80
HDRS 17 item		
Day 0 – baseline (n = 416)	22.34 $\pm$ 5.31	
Day 14 (n = 406)	18.80 $\pm$ 7.03	
Day 28 (n = 366)	15.61 $\pm$ 7.78	
Day 42 – end of the venlafaxine phase (n = 318)	14.43 $\pm$ 8.82	
Day 42 – baseline of the escitalopram phase (n = 154)		21.40 $\pm$ 6.13
Day 56 (n = 169)		18.22 $\pm$ 6.94
Day 70 (n = 163)		15.40 $\pm$ 7.50
Day 84 – end of the escitalopram phase (n = 157)		13.69 $\pm$ 8.33
CGI-S		
Day 0 – baseline (n = 415)	3.05 $\pm$ 3.54	
Day 14 (n = 406)	4.42 $\pm$ 1.11	
Day 28 (n = 366)	3.85 $\pm$ 1.29	
Day 42 – end of the venlafaxine phase (n = 318)	3.47 $\pm$ 1.58	
Day 42 – baseline of the escitalopram phase (n = 154)		4.78 $\pm$ 0.86
Day 56 (n = 169)		4.28 $\pm$ 1.15
Day 70 (n = 163)		3.79 $\pm$ 1.25
Day 84 – end of the escitalopram phase (n = 157)		3.30 $\pm$ 1.48
CGI-I		
Day 14 (n = 406)	3.47 $\pm$ 1.03	
Day 28 (n = 366)	2.94 $\pm$ 1.15	
Day 42 – end of the venlafaxine phase (n = 318)	2.79 $\pm$ 1.37	
Day 42 – baseline of the escitalopram phase (n = 154)		3.84 $\pm$ 0.87
Day 56 (n = 169)		3.30 $\pm$ 0.95
Day 70 (n = 163)		2.82 $\pm$ 1.08
Day 84 – end of the escitalopram phase (n = 157)		2.55 $\pm$ 1.28

Supplementary Table IV. Side effects of Completers in the two phases of the trial (n = 318 and n = 157, respectively).

Side effects (UKU)	Completers Venlafaxine Phase (n = 318) n(%)	Completers Escitalopram Phase (n = 157) n(%)
At least a psychic side effect (moderate-severe)		
Day 42 – end of the venlafaxine phase	120 (37.74)	
Day 84 – end of the escitalopram phase		52 (33.12)
At least a psychic side effect (severe)		
Day 42 – end of the venlafaxine phase	48 (15.09)	
Day 84 – end of the escitalopram phase		18 (11.46)
Psychic side effects (severe)		
Concentration Difficulties	25 (7.86)	8 (5.10)
Asthenia/Lassitude/Increased Fatigability	27 (8.49)	10 (6.37)
Sleepiness/Sedation	22 (6.92)	9 (5.73)
Failing Memory	0 (0.00)	0 (0.00)
Depression	23 (7.23)	8 (5.10)
Tension/Inner Unrest	10 (3.14)	1 (0.64)
Increased Duration of Sleep	2 (0.63)	4 (2.55)
Reduced Duration of Sleep	29 (9.12)	7 (4.46)
Increased Dream Activity	1 (0.31)	10 (6.37)
Emotional indifference	2 (0.63)	3 (1.91)
At least a neurologic side effect (moderate-severe)		
Day 42 – end of the venlafaxine phase	38 (11.95)	
Day 84 – end of the escitalopram phase		14 (8.92)
At least a neurologic side effect (severe)		
Day 42 – end of the venlafaxine phase	3 (0.94)	
Day 84 – end of the escitalopram phase		0 (0.00)
Neurologic side effects (severe)		
Dystonia	3 (0.94)	0 (0.00)
Rigidity	0 (0.00)	0 (0.00)
Hypokinesia/Akinesia	0 (0.00)	0 (0.00)
Hyperkinesia logic	0 (0.00)	0 (0.00)
Tremor	0 (0.00)	0 (0.00)
Akathisia	0 (0.00)	0 (0.00)
Epileptic Seizures	0 (0.00)	0 (0.00)
Paraesthesias	0 (0.00)	0 (0.00)
At least an autonomic side effect (moderate-severe)		
Day 42 – end of the venlafaxine phase	114 (35.85)	
Day 84 – end of the escitalopram phase		46 (29.30)
At least an autonomic side effect (severe)		
Day 42 – end of the venlafaxine phase	10 (3.14)	
Day 84 – end of the escitalopram phase		8 (5.09)
Autonomic side effects (severe)		
Accommodation Disturbances	1 (0.31)	0 (0.00)
Increased Salivation	0 (0.00)	0 (0.00)
Reduced Salivation	3 (0.94)	0 (0.00)
Nausea/Vomiting	0 (0.00)	0 (0.00)
Diarrhoea	0 (0.00)	1 (0.64)
Constipation	0 (0.00)	0 (0.00)
Micturition Disturbances	0 (0.00)	0 (0.00)
Polyuria/Polydipsia	0 (0.00)	0 (0.00)
Orthostatic Dizziness	0 (0.00)	0 (0.00)
Palpitations/Tachycardia	1 (0.31)	0 (0.00)
Increased Tendency to Sweating	5 (1.57)	7 (4.46)
At least another side effect (moderate-severe)		
Day 42 – end of the venlafaxine phase	117 (36.79)	
Day 84 – end of the escitalopram phase		65 (41.40)
At least another side effect (severe)		
Day 42 – end of the venlafaxine phase	40 (12.58)	
Day 84 – end of the escitalopram phase		17 (10.83)
Other side effects (severe)		
Rash	0 (0.00)	0 (0.00)
Pruritus	1 (0.31)	0 (0.00)

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Supplementary Table IV. (Continued)

Side effects (UKU)	Completers Venlafaxine Phase (n = 318) n(%)	Completers Escitalopram Phase (n = 157) n(%)
Photosensitivity	0 (0.00)	0 (0.00)
Increased Pigmentation	0 (0.00)	0 (0.00)
Weight gain	0 (0.00)	2 (1.27)
Weight loss	1 (0.31)	0 (0.00)
Menorrhagia	1 (0.31)	0 (0.00)
Amenorrhoea	1 (0.31)	0 (0.00)
Galactorrhoea	0 (0.00)	0 (0.00)
Gynaecomastia	0 (0.00)	0 (0.00)
Increased Sexual Desire	0 (0.00)	0 (0.00)
Diminished Sexual Desire	30 (9.43)	11 (7.01)
Erectile Dysfunction	6 (1.89)	4 (2.55)
Ejaculatory Dysfunction	6 (1.89)	2 (1.27)
Orgasmic Dysfunction	12 (3.77)	8 (5.09)
Dry Vagina	0 (0.00)	0 (0.00)
Headache	6 (1.89)	1 (0.64)
Physical Dependence	0 (0.00)	0 (0.00)
Psychic Dependence	0 (0.00)	0 (0.00)