

## **Supplementary Material**

Article Title: Brain-Volume Increase With Sustained Remission in Patients With Treatment-Resistant

**Unipolar Depression** 

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#### Supplementary eTable 1. Staging Score Methodology

Staging Method to Classify Retrospective<sup>a</sup> and Prospective<sup>b</sup> Degree of Treatment Resistance in Major Depressive Disorder

- (1) For each adequate trial of an antidepressant medication (6 weeks at or above minimum recommended dose), 1 point was assigned per trial.
- (2) For each optimization of dosage (treatment given at or above maximum recommended dose), an additional 0.5 points were assigned per trial.
- (3) For each medication added to a primary antidepressant as an augmentation or combination strategy (treatment given for at least 6 weeks regardless of the dosage), an additional 0.5 points were assigned per trial.
- (4) For each adequate trial of electroconvulsive therapy (at least nine sessions), an additional 3 points were assigned per trial.
- <sup>a</sup> Retrospective staging scores reflect treatment approaches taken during the five-year period preceding study enrollment. No points were assigned in retrospective chart reviews if trial dosage, time frame, or strategy was unclear.
- <sup>b</sup> Prospective staging scores were calculated from baseline visit to first remission visit. No points were assigned if drugs were discontinued due to side effects or noncompliance. Medication changes made during sustained remission were not included in calculations.

# Supplementary eTable 2. Minimum and Maximum Doses of Antidepressants and Other Medications Used in the Calculation of Staging Scores for Treatment Resistance

Drug Class Generic Name	Minimum Recommended Dose (mg/day)	Maximum Recommended Dose (mg/day)		
Tricyclic Antidepressants				
clomipramine amoxapine amitriptyline maprotiline desipramine nortriptyline doxepin trimipramine imipramine	150 150 150 100 150 75 150 150	250 250 250 250 250 125 250 250		
protriptyline	30	60		
Monoamine Oxidase Inhibitors (MAOIs)				
isocarboxazid phenelzine tranylcypromine maclobemide	30 45 30 300	60 90 60 900		
Selective Serotonin Reuptake Inhibitors (SSRIs)				
fluvoxamine paroxetine fluoxetine sertraline citalopram escitalopram	50 20 10 50 20 10	300 60 60 150 60 30		
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)				
venlafaxine duloxetine	125 60	250 100		
Norepinephrine Reuptake Inhibitor				
atomoxetine	40	100		

### Supplementary eTable 2 (cont.)

Drug Class Generic Name	Minimum Recommended Dose (mg/day)	Maximum Recommended Dose (mg/day)
Other Antidepressants		
trazodone nefazodone bupropion mirtazapine pinodolol topiramate	300 300 300 15 7.5 300	600 600 450 45 15 600
Atypical Antipsychotics		
quetiapine clozapine olanzapine ziprasidone aripiprazole paliperidone risperidone	50 25 5 40 5 1.5 0.25	600 100 20 100 30 9 4
Other Medications		
lithium triiodothyronine buspirone	600 0.025 20	1200 0.05 60
Dopamine agonists		
pramipexole bromocriptine	1 2.5	5 5

## Supplementary eTable 3. Treatment Approaches Used by Patients at Baseline and Follow-Up Imaging and Remission Status at Follow-Up $\,$

Patient	Baseline Treatment, Dosage (mg/day)	Follow-Up Treatment, Dosage (mg/day)	Status
1	citalopram 10, venlafaxine 225, quetiapine 50, trazodone 100	fluoxetine 40, quetiapine 300, trazodone 150	NR
2	venlafaxine 300, quetiapine 50, dextroamphetamine 20	tranylcypromine 20, atomoxetine 60	NR
3	venlafaxine 150	venlafaxine 150, bupropion 300	NR
4	escitalopram 10, atomoxetine 60, trazodone 100	bupropion 450, atomoxetine 60, trazodone 75	R
5	doxepin 300, flurazepam 30	venlafaxine 225, mirtazapine 30	NR
6	paroxetine 50	tranylcypromine 20, quetiapine 300	NR
7	fluoxetine 40, bupropion 300	fluoxetine 40, atomoxetine 25, trazodone 150	R
8	venlafaxine 300	moclobemide 900, bupropion 300	NR
9	venlafaxine 150, risperidone 0.5	venlafaxine 300, mirtazapine 45, pindolol 15, lamotrigine 100	R
10	bupropion 150	venlafaxine 300, bupropion 450	R
11	escitalopram 15, bupropion 150	escitalopram 30, buspirone 30, lithium 900, quetiapine 25	NR
12	paroxetine 50, trazodone 100	escitalopram 40, risperidone 2, lamotrigine 175	NR
13	venlafaxine 150, bupropion 150, trazodone 100	escitalopram 15, bupropion 150, mirtazapine 30	R
14	venlafaxine 300, amitriptyline 50, zopiclone 10	venlafaxine 300, amitriptyline 50, risperidone 2	NR
15	fluoxetine 40, clomipramine 50	escitalopram 10, bupropion 150, trazodone 100	R
16	venlafaxine 225, bupropion 300, risperidone 1	venlafaxine 300, nortriptyline 50, paliperidone 6	NR
17	moclobemide 750	escitalopram 40, pramipexole 3, bupropion 300	NR
18	paroxetine 20, bupropion 100, trazodone 50	paroxetine 20, bupropion 100, risperidone 1	R
19	paroxetine 20, amitriptyline 20, trazodone 150	paroxetine 40, pindolol 10, trazodone 150	R
20	paroxetine 60, mirtazapine 45, olanzapine 10, lithium 900	escitalopram 40, mirtazapine 60, buspirone 30, zopiclone 7.5	R
21	venlafaxine 225	venlafaxine 225, pindolol 10, trazodone 100	R
22	venlafaxine 225, olanzapine 10, trimipramine 100, temazepam 60, clonazepam 1, eltroxin 0.1	venlafaxine 150, ziprasidone 40, trimipramine 20 diazepam 20, levothyroxine 0.075	NR
23	citalopram 40, bupropion 150	escitalopram 20, atomoxetine 80, pramipexole 4, quetiapine 50	NR
24	venlafaxine 300, bupropion 150	venlafaxine 375	NR
25	escitalopram 20, bupropion 150, topiramate 100, temazepam 15	escitalopram 40, ziprasidone 40, pindolol 5, trazodone 100	NR
26	venlafaxine 187.5	venlafaxine 225, bupropion 450, trazodone 200	R
27	paroxetine 40, bupropion 150, trazodone 50	paroxetine 40, atomoxetine 40, modafinil 100, trazodone 150	R

Abbreviations: NR = nonremitter; R = Remitter