**SUPPLEMENTARY DIGITAL CONTENT**

**Trajectories of Function and Symptom Change in Desvenlafaxine Clinical Trials: Toward Personalized Treatment for Depression**

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Table S1: Desvenlafaxine studies for patients with major depressive disorder included in the pooled analysis. (Supplemental Digital Content 1.doc)

Table S2: Clinical and demographic characteristics of patients included in the pooled dataset. (Supplemental Digital Content 2.doc)

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## Table S1. Desvenlafaxine Studies for Patients With Major Depressive Disorder Included in the Pooled Analysis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID/ first author, yearRef [NCT identifier]** | **Eligibility criteria†** | **Study Duration (weeks)** | **Total Sample Size, N** | **Comparator** | | |  |
| **Desvenlafaxine 50 mg/d, n** | **Desvenlafaxine 100 mg/d, n** | **Other  Treatment Arms\*** | **Placebo, n** |
| 306 / DeMartinis et al, 20071 [NCT00072774] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 470 | – | 118 | Desvenlafaxine 200 mg/d, n = 116  Desvenlafaxine 400 mg/d, n = 116 | 120 |
| 332 / Liebowitz et al, 20082‑ [NCT00277823] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 451 | 151 | 148 | – | 152 |
| 333 / Boyer et al, 20083 [NCT00300378] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 485 | 166 | 158 | – | 161 |
| 335 / Tourian et al, 20094  [NCT00384033] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 616 | 148 | 150 | Duloxetine  60 mg/d, n = 157 | 161 |
| 4415 / Dunlop et al, 20115 [NCT00824291] | MADRS total score ≥25 | 12 | 427 | 285 | – | – | 142 |
| 3359 / Iwata et al, 20136 [NCT00798707] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 699 | 236 | – | Desvenlafaxine  25 mg/d, n = 232 | 231 |
| 3362 / Liebowitz et al, 20137 [NCT00863798] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 673 | 224 | – | Desvenlafaxine 10 mg/d, n = 226 | 223 |
| 3364 / Clayton et al, 20138 [NCT01121484] | MADRS total score ≥25 | 10 | 434 | 217 | – | – | 217 |
| 1028 / Clayton et al, 20159 [NCT01432457] | HAMD17 ≥20  HAMD17 (depressed mood) ≥2  CGI-S ≥4 | 8 | 909 | 300 | 309 | – | 300 |
| **Total sample size** | | | **5164** | **1727** | **883** | **847** | **1707** |

\*Data from these treatment arms were not included in the present analysis, which only used desvenlafaxine 50 mg or 100 mg treatment arms.   
†All patients had a DSM-VI diagnosis of MDD.

Abbreviations: CGI-S, Clinical Global Impressions– Severity of illness scale; HAMD, Hamilton Depression Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; NCT, ClinicalTrials.gov identifier.

**References**

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**Table S2.** Clinical and Demographic Characteristics of Patients Included in the analysis

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Desvenlafaxine**  **(n = 2610)** | **Placebo**  **(n = 1707)** | **Total Sample**  **(N = 4317)** |
| Age, y | 42.84 ± 12.99 | 42.98 ± 12.68 | 42.89 ± 12.87 |
| Male, % | 35.4 | 33.8 | 34.8 |
| Baseline HRSD | 23.24 ± 2.95 | 23.18 ± 3.01 | 23.21 ± 2.97 |
| Baseline SDS\* | 18.49 ± 6.02 | 18.29 ± 6.58 | 18.41 ± 6.26 |
| CGI-S score at baseline |  |  |  |
| Mildly or moderately ill† | 67.2% | 67.4% | 67.3% |
| Markedly or severely ill | 32.8% | 32.6% | 32.7% |

\*Total sample size for SDS is 3228 because not all patients had SDS data.

†Even though this category is labeled “mildly or moderately ill,” it also includes 2 patients whose baseline CGI-S score was reported as “borderline mentally ill.”

CGI-S, Clinical Global Impressions - Severity;HRSD, Hamilton Rating Scale for Depression; SDS, Sheehan Disability Scale.

## Table S3. Results From Model Selection for HRSD and SDS for the Placebo and Desvenlafaxine Groups

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Score** | **No. of Trajectories** | **Growth Mixture Model** | **Placebo** | | | | |  | **Desvenlafaxine** | | | | |
| **BIC** | **% Patients in Each Trajectory Class** | | | |  | **BIC** | **% Patients in Each Trajectory Class** | | | |
| **1** | **2** | **3** | **4** |  | **1** | **2** | **3** | **4** |
| **HRSD** | 1 | Linear | 60,671 | 100 | – | – | – |  | 92,666 | 100 | – | – | – |
| Log-linear | 59,076 | 100 | – | – | – |  | 89,768 | 100 | – | – | – |
| Quadratic | 58,560 | 100 | – | – | – |  | 89,033 | 100 | – | – | – |
| Cubic | 58,047 | 100 | – | – | – |  | 88,101 | 100 | – | – | – |
| 2 | Linear | 60,603 | 45.4 | 54.6 | – | – |  | 92,564 | 58.8 | 41.2 | – | – |
| Log-linear | 59,009 | 58.3 | 41.7 | – | – |  | 89,694 | 44.1 | 55.9 | – | – |
| Quadratic | 58,480 | 52 | 48 | – | – |  | 88,883 | 36.7 | 63.3 | – | – |
| Cubic | 57,967 | 50 | 50 | – | – |  | 87,950 | 35.4 | 64.6 | – | – |
| 3 | Linear | 60,595 | 5.6 | 51.2 | 43.2 | – |  | 92,551 | 49.7 | 41.2 | 9.1 | – |
| Log-linear | 58,999 | 7.1 | 52 | 40.8 | – |  | 89,668 | 48.7 | 8.4 | 42.9 | – |
| Quadratic | 58,454 | 19.7 | 37.2 | 43.1 | – |  | 88,868 | 15.2 | 48 | 36.8 | – |
| Cubic | **57,955** | **21.8** | **34.4** | **43.8** | **–** |  | 87,929 | 18.2 | 50.7 | 31.1 | – |
| 4 | Linear | 60,618 | 5.6 | 0 | 45 | 49.3 |  | 92,564 | 47 | 41.9 | 10.7 | 0.4 |
| Log-linear | 59,022 | 7.1 | 47.5 | 45.3 | 0 |  | 89,678 | 0.3 | 48 | 8.4 | 43.3 |
| Quadratic | 58,466 | 35 | 5.9 | 27.9 | 31.2 |  | 88,850 | 19.3 | 37.9 | 30.5 | 12.3 |
| Cubic | 57,950 | 24.2 | 8.2 | 25 | 42.6 |  | **87,904** | **37.6** | **12.5** | **16.9** | **33** |
| **SDS** | 1 | Linear | 34,585 | 100 |  |  |  |  | 49,530 | 100 |  |  |  |
| Log-linear | 34,222 | 100 |  |  |  |  | 48,905 | 100 |  |  |  |
| Quadratic | 34,181 | 100 |  |  |  |  | 48,908 | 100 |  |  |  |
| Cubic | 34,158 | 100 |  |  |  |  | 48,822 | 100 |  |  |  |
| 2 | Linear | 34,536 | 48.2 | 51.8 |  |  |  | 49,486 | 69.5 | 30.5 |  |  |
| Log-linear | 34,186 | 46.8 | 53.2 |  |  |  | 48,847 | 9.9 | 90.1 |  |  |
| Quadratic | 34,111 | 49.7 | 50.3 |  |  |  | 48,826 | 29.3 | 70.7 |  |  |
| Cubic | 34,094 | 50.2 | 49.8 |  |  |  | 48,738 | 29.5 | 70.5 |  |  |
| 3 | Linear | 34,512 | 14.9 | 52.7 | 32.4 |  |  | 49,450 | 41.1 | 22.9 | 36 |  |
| Log-linear | 34,139 | 33 | 53.5 | 13.5 |  |  | 48,811 | 17 | 44.3 | 38.7 |  |
| Quadratic | 34,115 | 38 | 36.2 | 25.9 |  |  | 48,760 | 12.4 | 53.1 | 34.4 |  |
| Cubic | 34,098 | 37.1 | 39.4 | 23.5 |  |  | **48,655** | **53.8** | **33.2** | **13** |  |
| 4 | Linear | 34,512 | 43.3 | 25.5 | 8.9 | 22.3 |  | 49,434 | 45.4 | 9.1 | 31.4 | 14.1 |
| Log-linear | 34,148 | 26.7 | 8.8 | 22.2 | 42.3 |  | 48,798 | 47.8 | 8 | 14.5 | 29.7 |
| Quadratic | 34,113 | 22.1 | 40.8 | 31 | 6.1 |  | 48,733 | 43.4 | 15.4 | 33.4 | 7.9 |
| Cubic | **34,022** | **11.2** | **36.7** | **32.4** | **19.6** |  | 48,628 | 42.9 | 15.6 | 32.5 | 9 |

**Table S4.** Percentage of Patients Receiving Similar Ranking for HRSD and SDS (Percentages Are Calculated Within HRSD Trajectories)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1. **Placebo Treatment** | | | | | | | | | | | | | | | | |
| **HRSD Trajectory** | | **SDS Trajectory Responders** | | **SDS Trajectory Non-responders** | | | | | | | | | **Total** | | | |
| **Moderate SDS Score at BL** | | | | | **Severe SDS Score at BL** | | | |
| **n** | **(%)** | **n** | | **(%)** | | | **n** | | **(%)** | | **n** | | **(%)** | |
| Fast responders | | 187 | (75) | 55 | | (22) | | | 8 | | (3) | | 250 | | (100) | |
| Partial responders | | 190 | (45) | 181 | | (43) | | | 50 | | (12) | | 421 | | (100) | |
| Non-responders | | 67 | (12) | 267 | | (49) | | | 211 | | (39) | | 545 | | (100) | |
| **Total** | | **444** | **(37)** | **503** | | **(41)** | | | **269** | | **(22)** | | **1216** | | **(100)** | |
| 1. **Desvenlafaxine Treatment** | | | | | | | | | | | | | | | | |
| **HRSD Trajectory** | **SDS Trajectory Responders** | | | | | |  | **SDS Trajectory Non-responders** | | | |  | **Total** | | |
| **n** | | | | **(%)** | |  | **n** | | **(%)** | |  | **n** | **(%)** | |
| Fast responders | 186 | | | | (85) | |  | 33 | | (15) | |  | 219 | (100) | |
| Slow responders | 557 | | | | (84) | |  | 110 | | (16) | |  | 667 | (100) | |
| Partial responders | 248 | | | | (49) | |  | 262 | | (51) | |  | 510 | (100) | |
| Non-responders | 59 | | | | (20) | |  | 243 | | (80) | |  | 302 | (100) | |
| **Total** | **1050** | | | | **(62)** | |  | **648** | | **(38)** | |  | **1698** | **(100)** | |
| Shading represents agreement between HRSD and SDS trajectory assignments. Percentages are based on the total number of patients in each HRSD trajectory. Patients assigned to the low baseline SDS trajectory were excluded from this table.  HRSD, Hamilton Rating Scale for Depression; SDS, Sheehan Disability Scale. | | | | | | | | | | | | | | | |