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eTable 1. Demographics and clinical characteristics of participants who completed study visits through week 12 vs non-completers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Completers (N=44) | Non-completers (N=14) | *t*/X2 |  *P* |
| SexWomen, N (%) | 17, (38.6) | 6, (42.9) | 0.78 (1) |  0.508 |
| RaceBlackWhiteHispanicAsianOther | 25 (56.8)17 (38.6)3 (6.8)1 (2.3)0 (0.0) | 7 (50.0)7 (50.0)2 (14.3)0 (0.0)0 (0.0) | 0.75 (1) |  0.348 |
| Age, mean (SD) | 47.60 (12.0) | 37.07 (11.0) | -2.91 |  0.005 |
| Education | 13.30 (2.7) | 12.79 (2.4) | -0.64 |  0.528 |
| Employment statusFull-timePart-timeUnemployed | 0 (0.0)11 (25.0)33 (75.0) | 1 (7.1)1 (7.1)12 (85.7) | 4.94 (2) | 0*.*085 |
| AP treatment, mean (SD) | (N=16)1807.06 (2233.8) | (N=4)886.00 (639.4) | -0.80 |  0.433 |
| PSYRATS Baseline, mean (SD) | 13.68 (4.2) | 10.79 (8.3) | -1.75 |  0.086 |
| SANS Baseline, mean (SD) | 31.73 (9.5) | 31.21 (11.1) | -0.16 |  0.867 |

Note: SD=standard deviation; t=t-test statistic for continuous variables; p=p-value; X2= Chi-square test statistic categorical variables; DUP=Duration of untreated psychosis; AP = Antipsychotic treatment

eTable 2. Medication use in randomized study sample

|  |  |  |
| --- | --- | --- |
|  | D-Cycloserine (N=30) | Placebo (N=28) |
| Antipsychotic Type, N (%) |  |  |
| First Generation  |  7 (23.3) |  8 (28.6) |
| Second Generation | 16 (53.3) | 15 (53.6) |
| Antipsychotic |  |  |
| Aripiprazole | 5 (16.7) | 3 (10.7) |
| Asenapine | 1 (3.3) | 0 (0.0) |
| Fluphenazine | 1 (3.3) | 4 (14.3) |
| Haloperidol | 3 (10.0) | 3 (10.7) |
| Lurasidone | 1 (3.3) | 0 (0.0) |
| Olanzapine | 4 (13.3) | 4 (14.3) |
| Paliperidone | 2 (6.7) | 0 (0.0) |
| Perphenazine | 3 (10.0) | 1 (3.6) |
| Risperidone | 0 (0.0) | 3 (10.7) |
| Quetiapine | 1 (3.3) | 3 (10.7) |
| Ziprasidone | 2 (6.7) | 2 (7.1) |
| Medication free | 9 (19.9) | 7 (25.0) |
|  |  |  |

eTable 3. Linear mixed model for repeated measures examining change in PSYRATS-D

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
|  | β, (SE) | 95% CI | *P* Value |
| **PSYRATS-D (N=53)** | **Model 1** |  |  |
| Baseline (week 3)a | -6.20, (3.88) | -14.09, 1.70 | 0.120 |
| Week 4 | .351, (.823) | -1.28, 1.98 | 0.671 |
| Week 6 | .151, (.823) | -1.48, 1.78 | 0.855 |
| Week 8 | .734, (.827) | -900, 2.37 | 0.376 |
| Week 10 | -.007, (.835) | -1.66, 1.65 | 0.993 |
| Week 12b | 11.49, (1.94) | 7.57, 15.42 | 0.001 |
| Group difference at Week 12 | -.797, (1.32) | -1.82, 3.42 | 0.547 |
| Information criteria Akaike | 1161.99 |  |  |
| **PSYRATS-D (N=49)** | **Model 2c** |  |  |
| Baseline (week 3)a | -6.37, (3.90) | -14.32, 1.59 | 0.113 |
| Week 4 | 1.04, (.799) | -.540, 2.62 | 0.195 |
| Week 6 | .996, (.799) | -.584, 2.58 | 0.215 |
| Week 8 | 1.36, (.804) | -.225, 2.95 | 0.092 |
| Week 10 | .624, (.831) | -1.02, 2.27 | 0.454 |
| Week 12b | 10.93, (1.94) | 6.99, 14.87 | 0.001 |
| Group difference at Week 12 | -.051, (1.33) | -2.70, 2.60 | 0.969 |
| Information criteria Akaike | 1053.39 |  |  |
| **PSYRATS-D (N=53)** | **Model 3d** |  |  |
| SANS baseline | 6.02, (6.09) | -8.01, 20.05 | 0.352 |
| Baseline (week 3)a | -4.01, (8.74) | -25.80, 17.78 | 0.664 |
| Week 4 | .126, (.843) | -1.54, 1.79 | 0.881 |
| Week 6 | -.040, (.843) | -1.71, 1.63 | 0.962 |
| Week 8 | .544, (.847) | -1.13, 2.22 | 0.522 |
| Week 10 | -.318, (.861) | -2.02, 1.39 | 0.712 |
| Week 12b | 11.12, (5.45) | -1.18, 23.41 | 0.071 |
| Group difference at Week 12 | -4.84, (2.09) | -9.69, .003 | 0.050 |
| Information criteria Akaike | .980.145 |  |  |
|  |  |  |  |

**Note:** aPSYRATS total at first administration of DCS (week 3) was included as a covariate in all models; bIntercept at week 12 represents the mean PSYRATS-D total for the reference group (DCS); Treatment group (Placebo, DCS) x study visit interaction terms were included in all models. Interactions were not significant; cModel 2, participants with SAPS < 3 at baseline were excluded from the analysis; dModel 3; SANS baseline score included as a covariate; all estimates and p-values refer to fixed effects in all models.

eTable 4. Linear regression examining change in distress (models 1-3) and perceived benefit of CBT (models 4-5) in predicting change on PSYRATS-D total score

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| **Change in level of distress following weekly CBT session**  | R2 | *Β* (SE) | *p* |
| **Model 1 – Change in PSYRATS-D from week 3-12**PSYRATS-D Week 3Average CBT ∆ distress∆ Distress x Group | 0.1930.218 | -0.468 (0.156)-0.018 (0.058)-0.061 (0.085) | 0.0050.7550.476 |
| **Model 2 – Change in PSYRATS-D from week 3-24**PSYRATS-D Week 3Average CBT ∆ distress∆ Distress x Group | 0.1900.298 | -0.412 (0.127)-0.034 (0.045)0.140 (0.062) | 0.0060.4590.031 |
| **Model 3 – Change in PSYRATS-D from week 3-36**PSYRATS-D Week 3Average CBT ∆ distress ∆ Distress x Group | 0.1630.198 | -0.488 (0.207)0.069 (0.066)-0.005 (0.092) | 0.0250.3030.960 |
| **Perceived benefit of weekly CBT session** |  |  |  |
| **Model 4 – Change in PSYRATS-D from week 3-12**PSYRATS-D Week 3Average perceived benefitAverage perceived benefit x group | 0.1930.200 | -0.451 (0.159)0.002 (0.043)0.008 (0.015) | 0.0070.9610.575 |
| **Model 5 – Change in PSYRATS-D from week 3-24**PSYRATS-D Week 3Average perceived benefitAverage perceived benefit x group | 0.1900.250 | -0.410 (0.129)-0.018 (0.036)-0.017 (0.011) | 0.0030.6140.136 |
| **Model 6 – Change in PSYRATS-D from week 3-36**PSYRATS-D Week 3Average perceived benefitAverage perceived benefit x group | 0.1630.194 | -0.501 (0.209)-0.051 (0.050)-0.005 (0.017) | 0.0220.3150.746 |

eTable 5. Treatment emergent side effects

|  |  |  |
| --- | --- | --- |
| **Symptom** | **Placebo** | **DCS** |
| Trouble sleeping | 10 | 5 |
| Nightmares or sleep disturbances | 8 | 6 |
| Drowsy or sleepy | 7 | 3 |
| Nervous or hyper | 2 | 5 |
| Weakness or fatigue | 11 | 4 |
| Irritable | 7 | 5 |
| Poor memory | 6 | 6 |
| Trouble concentrating | 7 | 5 |
| Feeling strange or unreal | 2 | 3 |
| Hearing or seeing things | 2 | 0 |
| Abnormal sensations | 2 | 3 |
| Numbness or tingling | 3 | 3 |
| Dizziness or faintness | 5 | 1 |
| Headache | 3 | 6 |
| Blurred vision | 5 | 2 |
| Ringing in ears or trouble hearing | 2 | 1 |
| Stuffy nose | 4 | 5 |
| Dry mouth | 4 | 2 |
| Drooling or increased salivation | 0 | 4 |
| Muscle cramps or stiffness | 12 | 4 |
| Muscle twitching or movements | 3 | 2 |
| Trouble sitting still | 0 | 2 |
| Tremor or shakiness | 2 | 1 |
| Poor coordination or unsteadiness | 2 | 1 |
| Slurred speech | 0 | 0 |
| Heartbeat rapid or pounding | 0 | 2 |
| Trouble catching breath or hyperventilating | 1 | 2 |
| Chest pain | 3 | 4 |
| Nausea or vomiting | 4 | 2 |
| Stomach or abdominal cramps | 3 | 5 |
| Constipation | 2 | 1 |
| Diarrhea | 2 | 4 |
| Difficulty starting urination | 2 | 3 |
| Frequent need to urinate | 5 | 5 |
| Menstrual irregularities | 0 | 0 |
| Loss of sexual interest | 3 | 4 |
| Problems with sexual arousal | 4 | 2 |
| Delayed or absent orgasm | 5 | 2 |
| Sweating excessively | 0 | 2 |
| Fluid retention or swelling | 1 | 0 |
| Appetite decreased | 1 | 0 |
| Appetite increased | 5 | 6 |
| Weight gain | 4 | 4 |
| Weight loss | 1 | 1 |
| Skin rash or allergy | 2 | 2 |
| Diminished mental acuity or sharpness | 8 | 5 |
| Difficulty finding words | 3 | 1 |
| Apathy emotional difference | 2 | 2 |
| Dizziness upon standing | 2 | 0 |
| Bruising | 0 | 1 |
| Hair thinning loss | 0 | 0 |
| Hot flashes | 2 | 2 |
| Clenching teeth at night | 1 | 2 |
| Straight taste in mouth | 1 | 0 |
| Unable to sit still | 0 | 2 |

**Note**: Side effects were assessed using the Systematic Assessment for Treatment Emergent Events (SAFTEE). Participant responses at each visit were compared to symptom responses at Week 2 (one week before baseline and the week prior to the start of medication administration). A side effect was defined as an increase of 2 points on an item on the SAFTEE. Individuals who reported a side effect in multiple weeks (i.e. at week 4 and 5) were only counted one time. Table reports the total number of participants reporting an increase in a side effect by 2 or more points on the SAFTEE at least one time during the study.