# Supplementary Tables and Figures:

### Supplementary Table 1: Descriptive statistics for the Calgary Depression Scale for Schizophrenia Sum score.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Time  (weeks) | N | Mean CDSS  Sum Score | Standard deviation | 95% Confidence interval | | | Skewness | Range |
| 0 | 138 | 6.71 | 5.18 | | 5.8-7.6 | 0.56 | | 0-19 |
| 1 | 127 | 5.80 | 4.92 | | 4.9-6.7 | 0.81 | | 0-19 |
| 3 | 119 | 4.86 | 4.35 | | 4.1-5.6 | 0.85 | | 0-16 |
| 6 | 98 | 4.73 | 4.51 | | 3.8-5.6 | 1.10 | | 0-17 |
| 12 | 85 | 4.48 | 4.30 | | 3.6-5.4 | 0.99 | | 0-17 |
| 26 | 69 | 4.11 | 4.43 | | 3.0-5.2 | 1.13 | | 0-18 |
| 39 | 64 | 3.28 | 4.12 | | 2.3-4.3 | 1.55 | | 0-18 |
| 52 | 62 | 4.05 | 4.81 | | 2.8-5.3 | 1.25 | | 0-21 |

CDSS (the Calgary Depression Scale for Schizophrenia)

### Supplementary Table 2: Latent contrast score model describing level and change in CDSS over time.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Weeks |  |  | Mean | P | SD |  |
| Baseline |  | I | 6.76 | <0.001 | 4.18 |  |
| 0-1 |  | S1 | -1.04 | 0.001 | 0.00 |  |
| 1-3 |  | S2 | -0.40 | 0.012 | 1.12 |  |
| 3-6 |  | S3 | -0.23 | 0.038 | 0.00 |  |
| 6-12 |  | S4 | 0.07 | 0.378 | 0.48 |  |
| 12-26 |  | S5 | -0.06 | 0.095 | 0.00 |  |
| 26-39 |  | S6 | -0.06 | 0.104 | 0.21 |  |
| 39-52 |  | S7 | 0.06 | 0.083 | 0.00 |  |

CDSS (Calgary Depression Scale for Schizophrenia).

Level and change presented at mean and individual level (SD: standard deviation) with p-values.

### Supplementary Table 3: Additional psychotropics in the more depressed (CDSS>6) vs. the less depressed (CDSS≤6) sub-cohort

**Intention to treat:**

In group with CDSS>6, N=68

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **Amisulpride (N=23)** | | | | **Aripiprazole (N=21)** | | | | **Olanzapine (N=23)** | | | | |
|  | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** |
|  | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** |
| baseline | 2 (8.7) | 1 (4.3) | 8 (3.8) | 0 | 3 (14.3) | **4 (19.0)** | 9 (42.9) | 0 | 6 (26.1) | 0 | 5 (21.7) | 1 (4.3) |
| 1 week | 2 (8.7) | 2 (8.7) | 8 (34.8) | 1 (4.3) | 3 (14.3) | 4 (20.0) | **12 (60.0)** | 0 | 6 (26.1) | 0 | 5 (21.7) | 1 (4.3) |
| 3 weeks | 4 (17.4) | 3 (13.0) | 12 (52.2) | 2 (8.7) | 3 (14.3) | 3 (14.3) | 10 (47.6) | 0 | 6 (27.3) | 1 (4.3) | 5 (21.7) | 1 (4.3) |
| 6 weeks | 4 (17.4) | 2 (8.7) | 5 (21.7) | 1 (4.3) | 4 (19.0) | 3 (14.3) | 10 (47.6) | 0 | 4 (17.4) | 0 | 5 (21.7) | 0 |
| 3 months | 3 (13.0) | 2 (8.7) | 3 (13.0) | **3 (13.0)** | 5 (23.8) | 2 (9.5) | 5 (23.8) | 0 | 5 (21.7) | 0 | 4 (17.4) | 0 |
| 6 months | 3 (13.0) | 3 (13.0) | 2 (8.7) | 0 | 4 (19.0) | 1 (4.8) | 3 (14.3) | 0 | 5 (21.7) | 0 | 3 (13.0) | 0 |
| 9 months | 2 (8.7) | 2 (8.7) | 1 (4.3) | 0 | 3 (15.0) | 1 (5.0) | 3 (15.0) | 0 | 3 (13.0) | 0 | 3 (13.0) | 1 (4.3) |
| 12 months | 3 (13.0) | 1 (4.3) | 1 (4.3) | 0 | 3 (15.0) | 1 (5.0) | 1 (5.0) | 0 | 3 (13.0) | 1 (4.3) | 2 (8.7) | 0 |

In group with CDSS<6 (N=70)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **Amisulpride (N=17)** | | | | **Aripiprazole (N=27)** | | | | **Olanzapine (N=26)** | | | | |
|  | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** |
|  | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** |
| baseline | 0 | 0 | 8 (47.1) | 1 (5.9) | 2 (7.4) | 1 (3.7) | 7 (25.9) | 0 | 0 | 0 | 9 (34.6) | 0 |
| 1 week | 0 | 0 | 8 (47.1) | 0 | 2 (7.4) | 0 | 5 (18.5) | 0 | 1 (4.0) | 0 | 7 (28.0) | 1 (4.0) |
| 3 weeks | 0 | 0 | 6 (35.3) | 0 | 1 (3.7) | 0 | 5 (18.5) | 1 (3.7) | 2 (7.7) | 0 | 6 (23.1) | 1 (3.8) |
| 6 weeks | 1 (5.9) | 0 | 5 (29.4) | 1 (5.9) | 1 (3.7) | 0 | 4 (14.8) | 1 (3.7) | 1 (3.8) | 1 (3.8) | 4 (15.4) | 0 |
| 3 months | 1 (5.9) | 0 | 1 (5.9) | 0 | 1 (3.8) | 0 | 2 (7.7) | 0 | 2 (7.7) | 1 (3.8) | 2 (7.7) | 0 |
| 6 months | 1 (5.9) | 0 | 0 | 0 | 2 (7.7) | 0 | 1 (3.8) | 0 | 0 | 0 | 0 | 0 |
| 9 months | 1 (5.9) | 0 | 0 | 0 | 2 (7.7) | 0 | 1 (3.8) | 0 | 0 | 0 | 1 (3.8) | 0 |
| 12 months | 1 (5.9) | 0 | 0 | 0 | 2 (8.0) | 0 | 2 (7.7) | 1 (3.8) | 1 (3.8) | 0 | 2 (7.7) | 1 (3.8) |

**Per protocol:**

In group with CDSS>6 (N=67)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **Amisulpride (N=28)** | | | | **Aripiprazole (N=23)** | | | | **Olanzapine (N=16)** | | | | |
|  | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** |
|  | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** |
| baseline | 4 (14.3) | 1 (3.6) | 9 (32.1) | 0 | 3 (13.0) | 4 (17.4) | 10 (43.5) | 1 (4.3) | 4 (25.0) | 0 | 3 (18.8) | 0 |
| 1 week | 4 (14.3) | 2 (7.1) | 9 (32.1) | 1 (3.6) | 3 (13.0) | 4 (18.2) | **13 (59.1)** | 1 (4.5) | 4 (25.0) | 0 | 3 (18.8) | 0 |
| 3 weeks | 6 (21.4) | 3 (10.7) | 12 (42.9) | 2 (7.1) | 3 (13.0) | 3 (13.0) | 11 (47.8) | 1 (4.3) | 4 (26.7) | 1 (6.3) | 4 (25.0) | 0 |
| 6 weeks | 6 (21.4) | 2 (7.1) | 7 (25.0) | 1 (3.6) | 4 (17.4) | 3 (13.0) | **11 (47.8)** | 0 | 2 (12.5) | 0 | 2 (12.5) | 0 |
| 3 months | 5 (17.9) | 2 (7.1) | 4 (14.3) | 3 (10.7) | 4 (17.4) | 2 (8.7) | 6 (26.1) | 0 | 4 (25.0) | 0 | 2 (12.5) | 0 |
| 6 months | 5 (17.9) | 3 (10.7) | 4 (14.3) | 0 | 3 (13.0) | 1 (4.3) | 3 (13.0) | 0 | 4 (25.0) | 0 | 1 (6.3) | 0 |
| 9 months | 3 (11.1) | 3 (11.1) | 2 (7.4) | 1 (3.7) | 3 (13.0) | 0 | 4 (17.4) | 0 | 2 (12.5) | 0 | 1 (6.3) | 0 |
| 12 months | 4 (14.8) | 3 (11.1) | 3 (11.1) | 0 | 3 (13.0) | 0 | 1 (4.3) | 0 | 2 (12.5) | 0 | 0 | 0 |

In group with CDSS<6 (N=70)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **Amisulpride (N=20)** | | | | **Aripiprazole (N=28)** | | | | **Olanzapine (N=22)** | | | | |
|  | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** | **AD** | **Mood** | **Bzd** | **Ach** |
|  | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** |
| baseline | 2 (10.0) | 0 | 11 (55.0) | 1 (5.0) | 0 | 1 (3.6) | 8 (28.6) | 0 | 0 | 0 | 5 (22.7) | 0 |
| 1 week | **3 (15.0)** | 0 | **11 (55.0)** | 0 | 0 | 0 | 5 (17.9) | 0 | 0 | 0 | 4 (19.0) | 1 (4.8) |
| 3 weeks | 2 (10.0) | 0 | **9 (45.0)** | 0 | 0 | 0 | 4 (14.3) | 1 (3.6) | 1 (4.5) | 0 | 4 (18.2) | 1 (4.5) |
| 6 weeks | 2 (10.0) | 0 | 7 (35.0) | 1 (5.0) | 0 | 0 | 3 (10.7) | 1 (3.6) | 1 (4.5) | 1 (4.5) | 3 (13.6) | 0 |
| 3 months | 1 (5.0) | 0 | 3 (15.0) | 0 | 0 | 0 | 0 | 0 | 3 (13.6) | 1 (4.5) | 2 (9.1) | 0 |
| 6 months | 2 (10.0) | 0 | 1 (5.0) | 0 | 0 | 0 | 0 | 0 | 1 (4.5) | 0 | 0 | 0 |
| 9 months | 2 (10.0) | 0 | 1 (5.0) | 0 | 0 | 0 | 0 | 0 | 1 (4.5) | 0 | 1 (4.5) | 0 |
| 12 months | 3 (15.0) | 0 | 1 (5.0) | 0 | 0 | 0 | 1 (3.7) | 1 (3.7) | 1 (4.5) | 0 | 2 (9.1) | 1 (4.5) |

AD: antidepressants; Mood: Mood stabilizers; Bzd: Benzodiazepines and anxiolytics/hypnotics; Ach: Anticholinergic drugs for side-effects. Statistically significant differences (p<0.05) are marked in bold font.

### Supplementary Figure 1: Linear model with medication differences - ITT analysis

ITT (Intention-to-treat), CDSS (Calgary Depression Scale for Schizophrenia)

### Supplementary Figure 2: Linear model with medication differences – Per Protocol analysis

CDSS (Calgary Depression Scale for Schizophrenia)

### Supplementary Figure 3: Latent contrast score model – Per Protocol

CDSS (Calgary Depression Scale for Schizophrenia)

### Supplementary Figure 4: Analysis restricted to de facto time on study drug - PP

CDSS (Calgary Depression Scale for Schizophrenia)

PP (per protocol-analysis)

### Supplementary Figure 5: Multi sample analysis – per protocol

CDSS (Calgary Depression Scale for Schizophrenia)

More depressed group: CDSS > 6 at baseline

Less depressed group: CDSS ≤ 6 at baseline

### Supplementary Figure 6: Missing data analysis

FIML=Full Information Maximum Likelihood; AUX=Auxilliary Variables model; MI=Multiple Imputation;

Diggle-Kenward=Diggle-Kenward model; Pattern-Mixture=Pattern-mixture model; Listwise=Listwise deletion