

## **SUPPLEMENTARY INFORMATION**

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## Supplementary table 1

### PANSS score decrease from baseline at each timepoint

|                       | Amisulpride (n=52) |              | Aripiprazole (n=51) |              | Olanzapine (n=41) |              |
|-----------------------|--------------------|--------------|---------------------|--------------|-------------------|--------------|
|                       | Men (n=25)         | Women (n=27) | Men (n=39)          | Women (n=12) | Men (n=29)        | Women (n=12) |
| <b>After 1 week</b>   |                    |              |                     |              |                   |              |
| PANSS total           | -16.3 (3.5)        | -7.3 (3.4)   | -8.6 (2.7)          | -6.3 (4.7)   | -10.1 (2.8)       | -5.5 (4.3)   |
| PANSS positive        | -5.6 (1.0)         | -3.5 (1.0)   | -2.7 (0.9)          | -1.4 (1.6)   | -2.7 (0.9)        | -1.7 (1.4)   |
| PANSS negative        | -2.7 (1.2)         | -0.55 (1.2)  | -2.1 (0.9)          | -0.9 (1.7)   | -1.4 (1.1)        | -1.4 (1.6)   |
| PANSS general         | -8.0 (1.9)         | -3.2 (1.9)   | -3.8 (1.5)          | -4.1 (2.7)   | -6.1 (1.6)        | -2.4 (2.4)   |
| <b>After 3 weeks</b>  |                    |              |                     |              |                   |              |
| PANSS total           | -22.2 (3.5)        | -16.2 (3.5)  | -12.8 (2.7)         | -10.1 (5.1)  | -19.4 (3.0)       | -11.7 (4.7)  |
| PANSS positive        | -7.0 (1.1)         | -6.7 (1.0)   | -4.2 (0.9)          | -4.0 (1.7)   | -6.5 (1.0)        | -2.8 (1.5)   |
| PANSS negative        | -3.4 (1.2)         | -1.5 (1.2)   | -3.0 (0.9)          | -0.9 (1.8)   | -2.5 (1.1)        | -3.4 (1.7)   |
| PANSS general         | -10.9 (1.9)        | -8.1 (1.9)   | -5.7 (1.5)          | -5.4 (2.9)   | -10.4 (1.7)       | -5.5 (2.6)   |
| <b>After 6 weeks</b>  |                    |              |                     |              |                   |              |
| PANSS total           | -25.2 (3.6)        | -19.2 (3.8)  | -14.9 (3.1)         | -15.0 (4.9)  | -18.0 (3.01)      | -17.1 (5.4)  |
| PANSS positive        | -9.3 (1.1)         | -7.2 (1.1)   | -6.8 (1.0)          | -4.6 (1.6)   | -7.1 (0.98)       | -5.6 (1.7)   |
| PANSS negative        | -3.5 (1.2)         | -1.5 (1.3)   | -0.5 (1.1)          | -2.7 (1.7)   | -0.9 (1.1)        | -4.8 (2.0)   |
| PANSS general         | -12.5 (2.0)        | -10.5 (2.1)  | -7.5 (1.8)          | -7.8 (2.8)   | -10.1 (1.7)       | -6.9 (3.0)   |
| <b>After 12 weeks</b> |                    |              |                     |              |                   |              |
| PANSS total           | -25.5 (3.8)        | -19.9 (4.0)  | -17.9 (3.3)         | -21.8 (5.5)  | -21.2 (3.1)       | -11.2 (5.4)  |
| PANSS positive        | -10.2 (1.1)        | -7.9 (1.2)   | -7.3 (1.1)          | -8.8 (1.9)   | -8.0 (1.0)        | -5.4 (1.7)   |
| PANSS negative        | -1.2 (1.3)         | -1.7 (1.4)   | -1.7 (1.2)          | -1.3 (1.9)   | -1.7 (1.2)        | -1.1 (2.0)   |
| PANSS general         | -14.2 (2.1)        | -10.3 (2.2)  | -8.9 (1.9)          | -11.9 (3.1)  | -11.6 (1.7)       | -4.8 (3.0)   |
| <b>After 26 weeks</b> |                    |              |                     |              |                   |              |
| PANSS total           | -34.4 (4.1)        | -18.8 (4.2)  | -18.8 (3.7)         | -27.7 (5.8)  | -18.7 (3.5)       | -13.0 (6.3)  |
| PANSS positive        | -13.3 (1.2)        | -7.5 (1.3)   | -7.9 (1.2)          | -11.5 (2.0)  | -7.8 (1.1)        | -6.2 (2.0)   |
| PANSS negative        | -4.7 (1.4)         | -1.7 (1.4)   | -1.1 (1.3)          | -2.3 (2.1)   | -1.5 (1.3)        | -1.2 (2.3)   |
| PANSS general         | -16.4 (2.3)        | -9.7 (2.3)   | -9.7 (2.1)          | -14.1 (3.3)  | -9.5 (1.9)        | -5.8 (3.5)   |
| <b>After 39 weeks</b> |                    |              |                     |              |                   |              |
| PANSS total           | -39.3 (4.1)        | -24.5 (4.0)  | -20.8 (3.9)         | -23.1 (9.1)  | -24.7 (3.5)       | -14.5 (6.3)  |
| PANSS positive        | -13.4 (1.2)        | -8.7 (1.2)   | -8.5 (1.3)          | -8.3 (3.0)   | -9.0 (1.1)        | -6.7 (2.0)   |
| PANSS negative        | -6.3 (1.4)         | -2.3 (1.4)   | -0.90 (1.4)         | -3.0 (3.2)   | -2.8 (1.3)        | -2.0 (2.3)   |
| PANSS general         | -19.7 (2.3)        | -13.4 (2.2)  | -11.3 (2.2)         | -12.1 (5.1)  | -13.0 (1.9)       | -6.0 (3.5)   |
| <b>After 52 weeks</b> |                    |              |                     |              |                   |              |
| PANSS total           | -38.9 (4.2)        | -19.7 (4.2)  | -23.2 (4.4)         | -24.1 (7.6)  | -25.3 (3.3)       | -23.2 (6.3)  |
| PANSS positive        | -13.3 (1.3)        | -7.9 (1.3)   | -10.9 (1.5)         | -8.2 (2.6)   | -8.3 (1.1)        | -8.2 (2.0)   |
| PANSS negative        | -6.7 (1.4)         | -2.3 (1.4)   | -1.5 (1.6)          | -3.7 (2.7)   | -3.7 (1.2)        | -6.5 (2.3)   |
| PANSS general         | -18.9 (2.3)        | -9.5 (2.3)   | -10.6 (2.5)         | -12.4 (4.3)  | -13.3 (1.8)       | -8.8 (3.5)   |

#### Notes

n=number in the total sample; PANSS=the Positive and Negative Syndrome Scale. Analysis based on linear mixed model with time as a categorical variable. PANSS score decrease at each timepoint is presented with SE.

## Supplementary table 2

### Comparison between medications for PANSS score reduction

|                | Men (n=93)         |                     |                      |                   |                      |
|----------------|--------------------|---------------------|----------------------|-------------------|----------------------|
|                | Amisulpride (n=25) | Aripiprazole (n=39) | p value <sup>1</sup> | Olanzapine (n=29) | p value <sup>2</sup> |
| PANSS total    | -0.60 (0.07)       | -0.35 (0.07)        | <b>0.014*</b>        | -0.33 (0.06)      | <b>0.004*</b>        |
| PANSS positive | -0.20 (0.02)       | -0.17 (0.02)        | 0.399                | -0.12 (0.02)      | <b>0.007*</b>        |
| PANSS negative | -0.10 (0.02)       | -0.00 (0.02)        | <b>&lt;0.001*</b>    | -0.05 (0.02)      | 0.057                |
| PANSS general  | -0.29 (0.04)       | -0.19 (0.04)        | <b>0.050</b>         | -0.16 (0.03)      | <b>0.011*</b>        |
|                | Women (n=51)       |                     |                      |                   |                      |
|                | Amisulpride (n=27) | Aripiprazole (n=12) | p value <sup>1</sup> | Olanzapine (n=12) | p value <sup>2</sup> |
| PANSS total    | -0.30 (0.06)       | -0.51 (0.13)        | 0.118                | -0.29 (0.11)      | 0.956                |
| PANSS positive | -0.11 (0.02)       | -0.21 (0.04)        | <b>0.032</b>         | -0.12 (0.04)      | 0.582                |
| PANSS negative | -0.04 (0.02)       | -0.06 (0.04)        | 0.591                | -0.06 (0.04)      | 0.609                |
| PANSS general  | -0.16 (0.03)       | -0.26 (0.07)        | 0.187                | -0.11 (0.06)      | 0.485                |

**Notes** n=number in the total sample; PANSS=the Positive and Negative Syndrome Scale. Analysis based on linear mixed model with time as continuous variable. PANSS score decrease per week is presented with SD. Amisulpride was used as reference category. P value<sup>1</sup>=amisulpride vs aripiprazole; p value<sup>2</sup>=amisulpride vs olanzapine. Differences significant with  $\alpha=0.05$  are shown in bold. P values with \* remained significant after FDR correction.

### Supplementary table 3

#### Comparison between medications for mean side-effects

|                                   | Men (n=93)         |                     |                   | p value          |
|-----------------------------------|--------------------|---------------------|-------------------|------------------|
|                                   | Amisulpride (n=25) | Aripiprazole (n=39) | Olanzapine (n=29) |                  |
| Neurologic side-effects (UKU)     | 0.37 (0.56)        | 0.46 (0.44)         | 0.34 (0.47)       | 0.155            |
| Sexual side-effects (UKU)         | 0.26 (0.42)        | 0.34 (0.43)         | 0.18 (0.35)       | <b>0.006</b>     |
| BMI increase (kg/m <sup>2</sup> ) | 0.90 (1.14)        | 0.64 (1.28)         | 1.48 (1.27)       | <b>&lt;0.001</b> |
| Glucose level (mmol/L)            | 5.08 (0.62)        | 5.71 (1.45)         | 5.40 (1.76)       | <b>0.001</b>     |
| Prolactin level (mIU/L)           | 920.3 (553.0)      | 265.9 (328.4)       | 376.5 (223.5)     | <b>&lt;0.001</b> |
| Tension in breasts (UKU)          | N/A                | N/A                 | N/A               | N/A              |
| Decreased menstruation (UKU)      | N/A                | N/A                 | N/A               | N/A              |

  

|                                   | Women (n=51)       |                     |                   | p value          |
|-----------------------------------|--------------------|---------------------|-------------------|------------------|
|                                   | Amisulpride (n=27) | Aripiprazole (n=12) | Olanzapine (n=12) |                  |
| Neurologic side-effects (UKU)     | 0.31 (0.38)        | 0.49 (0.40)         | 0.38 (0.46)       | <b>0.033</b>     |
| Sexual side-effects (UKU)         | 0.37 (0.48)        | 0.23 (0.44)         | 0.34 (0.54)       | 0.183            |
| BMI increase (kg/m <sup>2</sup> ) | 1.34 (2.27)        | -0.04 (1.46)        | 0.24 (1.25)       | <b>&lt;0.001</b> |
| Glucose level (mmol/L)            | 5.15 (0.82)        | 5.47 (1.63)         | 5.00 (0.68)       | 0.082            |
| Prolactin level (mIU/L)           | 1869.2 (1212.5)    | 307.4 (162.3)       | 667.7 (542.1)     | <b>&lt;0.001</b> |
| Tension in breasts (UKU)          | 0.17 (0.46)        | 0.25 (0.70)         | 0.02 (0.15)       | 0.078            |
| Decreased menstruation (UKU)      | 0.65 (1.15)        | 0.20 (0.66)         | 0.00 (0.00)       | <b>&lt;0.001</b> |

**Notes** n=number in the total sample; BMI=Body Mass index; kg=kilograms; mmol=millimole; mIU; milli International Units; L=litre. Analyses based on ANOVA. Data are mean values over all timepoints of the follow-up period with SD. Differences significant with  $\alpha=0.05$  are shown in bold. Post-hoc analyses were performed for significant group differences to evaluate differences between specific medication groups.

## Supplementary table 4

### Comparison between medications for side-effects post-hoc analyses

|                                   | Men (n=93)         |                     |                   | P value <sup>1</sup> | P value <sup>2</sup> | P value <sup>3</sup> |
|-----------------------------------|--------------------|---------------------|-------------------|----------------------|----------------------|----------------------|
|                                   | Amisulpride (n=25) | Aripiprazole (n=39) | Olanzapine (n=29) |                      |                      |                      |
| Neurologic side-effects (UKU)     | 0.37 (0.56)        | 0.46 (0.44)         | 0.34 (0.47)       | Not done             | Not done             | Not done             |
| Sexual side-effects (UKU)         | 0.26 (0.42)        | 0.34 (0.43)         | 0.18 (0.35)       | 0.267                | 0.225                | <b>0.004</b>         |
| BMI increase (kg/m <sup>2</sup> ) | 0.90 (1.14)        | 0.64 (1.28)         | 1.48 (1.27)       | 0.394                | <b>0.014</b>         | <b>&lt;0.001</b>     |
| Glucose level (mmol/L)            | 5.08 (0.62)        | 5.71 (1.45)         | 5.40 (1.76)       | <b>&lt;0.001</b>     | 0.145                | 0.173                |
| Prolactin level (mIU/L)           | 920.3 (553.0)      | 265.9 (328.4)       | 376.5 (223.5)     | <b>&lt;0.001</b>     | <b>&lt;0.001</b>     | <b>0.031</b>         |
| Tension in breasts (UKU)          | N/A                | N/A                 | N/A               |                      |                      |                      |
| Decreased menstruation (UKU)      | N/A                | N/A                 | N/A               |                      |                      |                      |

  

|                                   | Women (n=51)       |                     |                   | P value <sup>1</sup> | P value <sup>2</sup> | P value <sup>3</sup> |
|-----------------------------------|--------------------|---------------------|-------------------|----------------------|----------------------|----------------------|
|                                   | Amisulpride (n=27) | Aripiprazole (n=12) | Olanzapine (n=12) |                      |                      |                      |
| Neurologic side-effects (UKU)     | 0.31 (0.38)        | 0.49 (0.40)         | 0.38 (0.46)       | <b>0.025</b>         | 0.620                | 0.383                |
| Sexual side-effects (UKU)         | 0.37 (0.48)        | 0.23 (0.44)         | 0.34 (0.54)       | Not done             | Not done             | Not done             |
| BMI increase (kg/m <sup>2</sup> ) | 1.34 (2.27)        | -0.04 (1.46)        | 0.24 (1.25)       | <b>&lt;0.001</b>     | <b>0.041</b>         | 0.835                |
| Glucose level (mmol/L)            | 5.15 (0.82)        | 5.47 (1.63)         | 5.00 (0.68)       | Not done             | Not done             | Not done             |
| Prolactin level (mIU/L)           | 1869.2 (1212.5)    | 307.4 (162.3)       | 667.7 (542.1)     | <b>&lt;0.001</b>     | <b>&lt;0.001</b>     | 0.126                |
| Tension in breasts (UKU)          | 0.17 (0.46)        | 0.25 (0.70)         | 0.02 (0.15)       | Not done             | Not done             | Not done             |
| Decreased menstruation (UKU)      | 0.65 (1.15)        | 0.20 (0.66)         | 0.00 (0.00)       | <b>0.017</b>         | <b>&lt;0.001</b>     | 0.598                |

**Notes** n=number in the total sample; BMI=Body Mass index; kg=kilograms; mmol=millimole; mIU; milli International Units; L=litre. Analyses based on Tukey's post-hoc tests. Data are mean values over all timepoints of the follow-up period with SD. Differences significant with  $\alpha=0.05$  are shown in bold. p value<sup>1</sup>=amisulpride vs. aripiprazole, p value<sup>2</sup>=amisulpride vs. olanzapine, p value<sup>3</sup>=aripiprazole vs. olanzapine. Not done=post-hoc analysis not done, because no significant differences in ANOVA.

## Supplementary data

### R codes

```
# Simplified version of syntaxes that have been used in the analyses

# Load required libraries

library(devEMF)

library(dplyr)

library(haven)

library(lsmmeans)

library(nlme)

# Commands used for reading and preparing data have been removed

# Modell 1, Comparison between men and women for PANSS score reduction, time as
continuous variable

data$time = as.numeric(data$time)

modell1 = lme(panss ~ time + gender + time:gender, random = ~1|Patient_ID, data=data)

# Comparison between men and women for mean side-effects

group_by(data, gender) %>% summarise(mean=mean(side_effect), sd=sd(side_effect))

# Modell 2, Comparison between men and women for PANSS score reduction, time as
categorical variable

data$time = as.factor(data$time)

modell2 = lme(panss ~ time + gender + time:gender, random = ~1|Patient_ID, data=data)

# Comparison between medications for mean side-effects

group_by(data, medication) %>% summarise(mean=mean(side_effect), sd=sd(side_effect))

# Commands used for storing tables and figures have been removed
```