**Supplementary material 1 Flow diagram**

Analysed Intention To Treat (n=52) Analysed Per Protocol (n=41)

Analysed Intention To Treat (n=48) Analysed Per Protocol (n=51)

Analysed Intention To Treat (n=44) Analysed Per Protocol (n=52)

Week

52

Sum

Week

39

Week

26

Week

12

Week

6

Week

3

Week

1

Lost to follow-up (n=27) Discontinued study drug

Stopped antipsychotic drug (n=9)

Changed antipsychotic drug (n=8)

Change to depot (n=3)

Protocol violation (n=2)

Drop out (n=22)

Lost to follow-up (n=35) Discontinued study drug

Stopped antipsychotic drug (n=2)

Changed antipsychotic drug (n=12)

Change to depot (n=0)

Protocol violation (n=0)

Drop out (n=25)

Lost to follow-up (n=22) Discontinued study drug

Stopped antipsychotic drug (n=4)

Changed antipsychotic drug (n=9)

Change to depot (n=0)

Protocol violation (n=1)

Drop out (n=17)

Lost to follow-up (n=27) Discontinued study drug (n=21)

Lost to follow-up (n=34) Discontinued study drug (n=14)

Lost to follow-up (n=20) Discontinued study drug (n=13)

Lost to follow-up (n=27) Discontinued study drug (n=14)

Lost to follow-up (n=27) Discontinued study drug (n=13)

Lost to follow-up (n=20) Discontinued study drug (n=12)

Lost to follow-up (n=20) Discontinued study drug (n=10)

Lost to follow-up (n=23) Discontinued study drug (n=11)

Lost to follow-up (n=17) Discontinued study drug (n=7)

Lost to follow-up (n=15) Discontinued study drug (n=6)

Lost to follow-up (n=20) Discontinued study drug (n=9)

Lost to follow-up (n=6) Discontinued study drug (n=2)

Lost to follow-up (n=10) Discontinued study drug (n=3)

Lost to follow-up (n=9) Discontinued study drug (n=4)

Lost to follow-up (n=10) Discontinued study drug (n=6)

Lost to follow-up (n=4) Discontinued study drug (n=2)

Lost to follow-up (n=5) Discontinued study drug (n=2)

Allocated to **olanzapine** (n=52)

Received allocated study drug (n=39)

Chose another study drug (n=13)

Amisulpride (n=9)

Aripiprazole (n=4)

Allocated to **aripiprazole** (n=48)

Received allocated study drug (n=43)

Chose another study drug (n=5)

Amisulpride (n=5)

Olanzapine (n=0)

## Enrollment

Randomized (n=144)

## Follow-Up

## Analysis

## Allocation

Allocated to **amisulpride** (n=44)

Received allocated study drug (n=38)

Chose another study drug (n=6) Aripiprazole (n=4)

Olanzapine (n=2)

Lost to follow-up (n=6) Discontinued study drug (n=1)

Excluded (n=215)

  Not meeting inclusion criteria (n=107)

  Declined to participate (n=82)

  Other reasons (n=26)

Assessed for eligibility (n=359)

**Notes**

Lost to follow up=explicit withdrawal from further participation in the study or not showing up at subsequent study visits; Depot=long-acting formulation of study drug; Protocol violation=use of dosage above upper limit according to the study protocol; Drop out=unknown study drug use status because participant is lost to follow-up.

**Supplementary material S2**

Baseline demographic and clinical characteristics for the hallucinating (HALL) sub-group, ITT

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Amisulpride (N=33) | Aripiprazole (N=33) | Olanzapine (N=39) | All (N=105) |
|  | n (SD or %) | n (SD or %) | n (SD or %) | n (SD or %) |
| Age | 29.8 (11.8) | 33.9 (14.5) | 31.4 (13.1) | 31.7 (13.1) |
| Men | 19/33 (58%) | 20/33 (61%) | 24/39 (62%) | 63/105 (60%) |
| White | 28/33 (85%) | 23/33 (70%) | 31/39 (79%) | 82/105 (78%) |
| Years of education | 12 (2.6) | 11.9 (3.2) | 11.8 (2.6) | 11.9 (2.8) |
| Living alone | 16/33 (48%) | 14/33 (42%) | 14/39 (36%) | 44/105 (42%) |
| Employed | 9/33 (27%) | 7/33 (21%) | 8/39 (21%) | 24/105 (23%) |
| Smoking | 20/33 (61%) | 19/33 (58%) | 21/39 (54%) | 60/105 (57%) |
| Alcohol abuse/dependence | 3/33 (9%) | 5/33 (15%) | 2/39 (5%) | 10/105 (10%) |
| Drug abuse/dependence | 8/33 (24%) | 4/33 (12%) | 8/39 (21%) | 20/105 (19%) |
| Diagnosis: Schizophrenia | 23/33 (70%) | 21/33 (64%) | 24/39 (62%) | 68/105 (65%) |
| Diagnosis: Schizotypal | 1/33 (3%) | 0/33 (0%) | 1/39 (3%) | 2/105 (2%) |
| Diagnosis: Delusional disorder | 2/33 (6%) | 4/33 (12%) | 4/39 (10%) | 10/105 (10%) |
| Diagnosis: Brief psychotic disorder | 4/33 (12%) | 1/33 (3%) | 4/39 (10%) | 9/105 (9%) |
| Diagnosis: Schizo-affective | 3/33 (9%) | 4/33 (12%) | 2/39 (5%) | 9/105 (9%) |
| Diagnosis: Other | 0/33 (0%) | 1/33 (3%) | 0/39 (0%) | 1/105 (1%) |
| Diagnosis: Unspecified | 0/33 (0%) | 2/33 (6%) | 4/39 (10%) | 6/105 (6%) |
| APnaive (AP-) | 13/33 (39%) | 17/33 (52%) | 16/39 (41%) | 46/105 (44%) |
| PANSS total | 83.2 (18.8) | 80.9 (11.7) | 79.9 (16) | 81.3 (15.7) |
| PANSS positive | 22.5 (4.7) | 22.8 (4.6) | 21.3 (5.1) | 22.2 (4.8) |
| PANSS negative | 18.6 (6.9) | 18.1 (5) | 18.3 (6) | 18.3 (6) |
| PANSS general | 42.1 (10.3) | 40 (7) | 40.3 (8.1) | 40.8 (8.5) |
| CGI | 5.2 (0.9) | 5 (0.8) | 5.1 (0.8) | 5.1 (0.8) |
| GAF | 35.1 (9.4) | 35.1 (8.1) | 34.8 (8.9) | 35 (8.7) |
| CDSS | 7.9 (6.1) | 6.5 (4.5) | 7.3 (5.3) | 7.2 (5.3) |

N=number in the HALL sub-group; n=number with characteristics; Smoking=daily tobacco smokers; AP naïve=no previous exposure to antipsychotic drugs; PANSS=the Positive and Negative Syndrome Scale; CGI=the Clinical Global Impression severity of illness scale; GAF=Global Assessment of Functioning scale-split version; CDSS= the Calgary Depression Scale for Schizophrenia

**Supplementary material S3**

Table S3-1

PANSS P3 for each medication, all participants included - ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| All patients | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=44) | 3.68 (0.236) | -0.69 (0.247) | -1.32 (0.246) | -1.67 (0.256) | -1.76 (0.272) | -2.03 (0.294) | -2.18 (0.285) | -2.1  (0.294) |
| Aripiprazole (n=48) | 3.5  (0.226) [p=0.58] | -0.46 (0.234) [p=0.457] | -0.71  (0.24) [p=0.053] | -1.31 (0.265) [p=0.289] | -1.38 (0.275) [p=0.296] | -1.85 (0.291) [p=0.647] | -1.81 (0.327) [p=0.378] | -2.24 (0.355) [p=0.755] |
| Olanzapine (n=52) | 3.73 (0.217) [p=0.877] [[p=0.877]] | -0.72 (0.222) [p=0.94] [[p=0.387]] | -1.27 (0.231) [p=0.885] [[p=0.064]] | -1.31 (0.239) [p=0.263] [[p=0.998]] | -1.3  (0.25) [p=0.174] [[p=0.795]] | -1.39 (0.277) [p=0.091] [[p=0.221]] | -1.54 (0.277) [p=0.089] [[p=0.5]] | -1.54  (0.27) [p=0.133]  [[p=0.1]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S3-2

PANSS P3 for each medication, all participants included - PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=52) | 4.02 (0.217) | -0.8 (0.223) | -1.47 (0.225) | -1.58  (0.235) | -1.7  (0.247) | -2.07 (0.263) | -2.12 (0.257) | -1.93 (0.266) |
| Aripiprazole (n=51) | 3.24 (0.219) **[p=0.012]** | -0.35 (0.229) [p=0.123] | -0.66 (0.232) **[p=0.006]** | -1.34  (0.251) [p=0.455] | -1.23 (0.268) [p=0.162] | -1.54 (0.293) [p=0.156] | -1.46 (0.333) [p=0.101] | -2.05 (0.353) [p=0.789] |
| Olanzapine (n=41) | 3.66 (0.244) [p=0.272] [[p=0.271]] | -0.76 (0.252) [p=0.913] [[p=0.18]] | -1.17 (0.265) [p=0.352] [[p=0.114]] | -1.35  (0.276) [p=0.491] [[p=0.983]] | -1.46 (0.283) [p=0.483] [[p=0.525]] | -1.55 (0.313) [p=0.175] [[p=0.991]] | -1.81 (0.313) [p=0.417] [[p=0.425]] | -1.82 (0.303) [p=0.763] [[p=0.609]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

**Supplementary material S4**

PANSS P3 for each medication, HALL sub-group. PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=42) | 4.67 (0.219) | -0.96  (0.225) | -1.85 (0.228) | -1.95 (0.244) | -2.17  (0.253) | -2.53 (0.277) | -2.54 (0.268) | -2.31  (0.282) |
| Aripiprazole (n=32) | 4.44  (0.25) [p=0.493] | -0.59  (0.263) [p=0.279] | -1.22 (0.263) [p=0.071] | -2.15 (0.28) [p=0.587] | -2.21  (0.312) [p=0.926] | -2.37 (0.326) [p=0.711] | -1.98 (0.397) [p=0.241] | -3.03  (0.44) [p=0.167] |
| Olanzapine (n=31) | 4.39 (0.254) [p=0.407] [[p=0.406]] | -1.01  (0.26) [p=0.899] [[p=0.258]] | -1.43 (0.273) [p=0.242] [[p=0.574]] | -1.71 (0.285) [p=0.526] [[p=0.271]] | -1.82  (0.29) [p=0.366] [[p=0.365]] | -1.86 (0.326) [p=0.118] [[p=0.268]] | -2.18 (0.312) [p=0.376] [[p=0.695]] | -2.18  (0.312) [p=0.767] [[p=0.116]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

**Supplementary material S5**

Table S5-1

PANSS P3 for each medication, HALL sub-group, AP-, ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=13) | 4.54 (0.396) | -0.99 (0.407) | -1.38 (0.431) | -1.82 (0.448) | -1.9 (0.491) | -2.26 (0.522) | -2.26 (0.522) | -2.42 (0.522) |
| Aripiprazole (n=17) | 4.59 (0.346) [p=0.925] | -0.79 (0.354) [p=0.719] | -1.42 (0.354) [p=0.951] | -1.87 (0.403) [p=0.939] | -1.74 (0.417) [p=0.808] | -2.43 (0.433) [p=0.802] | -2.15 (0.505) [p=0.885] | -3.14 (0.543) [p=0.348] |
| Olanzapine (n=16) | 4.19 (0.357) [p=0.513] [[p=0.511]] | -1.38 (0.357) [p=0.488] [[p=0.257]] | -1.46 (0.372) [p=0.902] [[p=0.943]] | -1.59 (0.405) [p=0.707] [[p=0.631]] | -2.09 (0.419) [p=0.772] [[p=0.561]] | -2.41 (0.454) [p=0.822] [[p=0.982]] | -2.41 (0.454) [p=0.824] [[p=0.703]] | -2.19 (0.454) [p=0.744] [[p=0.186]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S5-2

PANSS P3 for each medication, HALL sub-group, AP-, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=14) | 4.5  (0.378) | -1  (0.388) | -1.21 (0.409) | -1.68 (0.46) | -1.41 (0.514) | -2.15 (0.554) | -1.75 (0.554) | -1.95 (0.554) |
| Aripiprazole (n=17) | 4.59 (0.343) [p=0.864] | -0.79 (0.351) [p=0.704] | -1.42 (0.351) [p=0.709] | -1.87 (0.399) [p=0.762] | -1.74 (0.413) [p=0.617] | -2.43 (0.43) [p=0.699] | -2.15 (0.501) [p=0.6] | -3.14 (0.538) [p=0.13] |
| Olanzapine (n=15) | 4.2  (0.365) [p=0.571] [[p=0.569]] | -1.4 (0.365) [p=0.459] [[p=0.241]] | -1.63 (0.382) [p=0.467] [[p=0.691]] | -1.73 (0.393) [p=0.939] [[p=0.805]] | -2.38 (0.405) [p=0.146] [[p=0.281]] | -2.47 (0.434) [p=0.658] [[p=0.947]] | -2.7 (0.434) [p=0.185] [[p=0.411]] | -2.51 (0.434) [p=0.439] [[p=0.365]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

**Supplementary material S6**

PANSS P3 for each medication, HALL sub-group, AP+, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=28) | 4.75 (0.262) | -0.95 (0.27) | -2.14 (0.27) | -2.08 (0.284) | -2.44 (0.288) | -2.69 (0.315) | -2.81 (0.303) | -2.46 (0.322) |
| Aripiprazole (n=15) | 4.27 (0.358) [p=0.282] | -0.32 (0.387) [p=0.182] | -0.96 (0.388) **[p=0.012]** | -2.38 (0.388) [p=0.525] | -2.88 (0.468) [p=0.427] | -2.3 (0.495) [p=0.508] | -1.64 (0.653) [p=0.104] | -2.78 (0.776) [p=0.704] |
| Olanzapine (n=16) | 4.56 (0.347) [p=0.67] [[p=0.668]] | -0.59 (0.363) [p=0.424] [[p=0.61]] | -1.19 (0.383) **[p=0.041**] [[p=0.671]] | -1.72 (0.407) [p=0.46] [[p=0.231]] | -1.23 (0.407) **[p=0.015] [[p=0.007]]** | -1.02 (0.488) **[p=0.004] [[p=0.063]]** | -1.57  (0.44) **[p=0.02]** [[p=0.925]] | -1.82  (0.44) [p=0.233] [[p=0.277]] |

AP+ participants exposed to antipsychotic treatment before entering the study; Numbers in the baseline column gives the estimated values; numbers in the other columns gives the estimated decrease in PANSS P3 compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; p values in double brackets corresponds to comparison to aripiprazole

**Supplementary material S7**

Table S7-1

PANSS P3 for Olanzapine, HALL sub-group, ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| AP+ (n=23) | 4.74 (0.306) | -0.61 (0.318) | -1.7 (0.323) | -1.74 (0.333) | -1.4 (0.339) | -1.23 (0.379) | -1.59 (0.353) | -1.71 (0.36) |
| AP-(n=16) | 4.19 (0.366) [p=0.255] | -1.37 (0.366) [p=0.083] | -1.47 (0.379) [p=0.614] | -1.56 (0.406) [p=0.711] | -2.08 (0.418) [p=0.179] | -2.4  (0.448) **[p=0.034]** | -2.41 (0.448) [p=0.124] | -2.19 (0.448) [p=0.373] |

AP+ participants exposed to antipsychotic treatment before entering the study; AP- no previous exposure to antipsychotic drugs (antipsychotic naïve); Numbers in the baseline column gives the estimated values; numbers in the other columns gives the estimated decrease in PANSS P3 compared to baseline; Numbers in parentheses are estimated standard deviations (SD); Numbers in brackets are p values.

Table S7-2

PANSS P3 for Olanzapine, HALL sub-group, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| AP+ (n=16) | 4.56 (0.359) | -0.6 (0.374) | -1.2  (0.393) | -1.72 (0.414) | -1.24 (0.415) | -1.03  (0.49) | -1.57 (0.446) | -1.82 (0.446) |
| AP- (n=15) | 4.2 (0.371) [p=0.488] | -1.4 (0.371) [p=0.105] | -1.64 (0.385) [p=0.397] | -1.72 (0.394) [p=0.999] | -2.38 (0.405) **[p=0.038]** | -2.48 (0.429) **[p=0.022]** | -2.72 (0.43) [p=0.053] | -2.52  (0.43) [p=0.238] |

AP+ participants exposed to antipsychotic treatment before entering the study; AP- no previous exposure to antipsychotic drugs (antipsychotic naïve); Numbers in the baseline column gives the estimated values; numbers in the other columns gives the estimated decrease in PANSS P3 compared to baseline; Numbers in parentheses are estimated standard deviations (SD); Numbers in brackets are p values.

**Supplementary material S8**

Sub-group of participants with PANSS P3 ≥4

*Overall analysis*

Table S8-1

PANSS P3 for each medication, participants with P3 ≥4, ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=26) | 4.85 (0.265) | -0.95 (0.274) | -1.98 (0.281) | -2.39 (0.303) | -2.97 (0.324) | -2.91 (0.353) | -3.2 (0.333) | -3.13 (0.354) |
| Aripiprazole (n=29) | 4.76 (0.251) [p=0.811] | -0.78 (0.259) [p=0.681] | -1.43 (0.262) [p=0.174] | -2.15 (0.283) [p=0.585] | -2.08 (0.306) [p=0.055] | -2.61 (0.313) [p=0.547] | -2.35 (0.376) [p=0.1] | -2.95 (0.413) [p=0.758] |
| Olanzapine (n=30) | 4.97 (0.247) [p=0.74] [[p=0.74]] | -0.95 (0.253) [p=0.999] [[p=0.67]] | -1.61 (0.26) [p=0.349] [[p=0.655]] | -1.73 (0.276) [p=0.125] [[p=0.308]] | -1.68 (0.272) **[p=0.004]** [[p=0.348]] | -1.86 (0.31) **[p=0.032]** [[p=0.1]] | -2.17 (0.291) **[p=0.025]** [[p=0.715]] | -2.02 (0.291) **[p=0.02]** [[p=0.072]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S8-2

PANSS P3 for each medication, participants with P3 ≥4, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=35) | 4.97 (0.233) | -0.99 (0.238) | -1.97 (0.243) | -2.06 (0.266) | -2.38 (0.271) | -2.67 (0.29) | -2.77 (0.28) | -2.53 (0.296) |
| Aripiprazole (n=27) | 4.7  (0.265) [p=0.45] | -0.66 (0.277) [p=0.385] | -1.47 (0.277) [p=0.196] | -2.35 (0.296) [p=0.481] | -2.21 (0.338) [p=0.71] | -2.41 (0.348) [p=0.581] | -1.94 (0.422) [p=0.111] | -3.15 (0.477) [p=0.282] |
| Olanzapine (n=23) | 4.87 (0.287) [p=0.784] [[p=0.784]] | -0.99 (0.292) [p=0.999] [[p=0.431]] | -1.41 (0.307) [p=0.169] [[p=0.881]] | -1.75 (0.32) [p=0.48] [[p=0.187]] | -1.86 (0.314) [p=0.234] [[p=0.467]] | -2.07 (0.363) [p=0.214] [[p=0.513]] | -2.57 (0.343) [p=0.661] [[p=0.26]] | -2.37 (0.335) [p=0.734] [[p=0.194]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

*Analyses for AP- and AP+ participants*

Table S8-3

PANSS P3 for each medication, participants with P3 ≥4, AP-, ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=10) | 5 (0.434) | -1.08 (0.452) | -1.56 (0.495) | -2.07 (0.526) | -2.5 (0.62) | -2.45 (0.568) | -2.85 (0.568) | -3.05 (0.568) |
| Aripiprazole (n=16) | 4.69 (0.343) [p=0.576] | -0.71 (0.353) [p=0.548] | -1.51 (0.353) [p=0.94] | -1.94 (0.41) [p=0.853] | -1.67 (0.427) [p=0.291] | -2.44 (0.427) [p=0.984] | -2.16 (0.501) [p=0.384] | -3.16 (0.54) [p=0.893] |
| Olanzapine (n=10) | 4.9  (0.434) [p=0.872] [[p=0.872]] | -1.6 (0.434) [p=0.437] [[p=0.137]] | -1.46 (0.45) [p=0.893] [[p=0.939]] | -1.35 (0.525) [p=0.364] [[p=0.407]] | -2.14 (0.496) [p=0.663] [[p=0.498]] | -2.72 (0.525) [p=0.742] [[p=0.691]] | -3.02 (0.525) [p=0.835] [[p=0.258]] | -2.43 (0.496) [p=0.431] [[p=0.337]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S8-4

PANSS P3 for each medication, participants with P3 ≥4, AP-, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=11) | 4.91 (0.412) | -1.08 (0.427) | -1.32 (0.464) | -1.87 (0.562) | -1.7  (0.7) | -2.28 (0.62) | -2.28 (0.62) | -2.53  (0.62) |
| Aripiprazole (n=16) | 4.69 (0.342) [p=0.681] | -0.71 (0.351) [p=0.534] | -1.51 (0.351) [p=0.767] | -1.94 (0.409) [p=0.929] | -1.67 (0.426) [p=0.972] | -2.43 (0.426) [p=0.847] | -2.16 (0.501) [p=0.886] | -3.16  (0.54) [p=0.461] |
| Olanzapine (n=9) | 5  (0.455) [p=0.883] [[p=0.883]] | -1.67 (0.455) [p=0.386] [[p=0.123]] | -1.74 (0.474) [p=0.555] [[p=0.711]] | -1.67 (0.499) [p=0.806] [[p=0.704]] | -2.6 (0.475) [p=0.313] [[p=0.174]] | -2.84 (0.498) [p=0.509] [[p=0.565]] | -3.39 (0.499) [p=0.188] [[p=0.101]] | -2.85 (0.475) [p=0.703] [[p=0.678]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S8-5

PANSS P3 for each medication, participants with P3 ≥4, AP+, ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=16) | 4.75 (0.328) | -0.88 (0.337) | -2.21 (0.337) | -2.56 (0.365) | -3.17 (0.376) | -3.21 (0.447) | -3.38 (0.406) | -3.15  (0.447) |
| Aripiprazole (n=13) | 4.85 (0.364) [p=0.845] | -0.88 (0.376) [p=1] | -1.32 (0.388) [p=0.104] | -2.35 (0.387) [p=0.71] | -2.52 (0.436) [p=0.285] | -2.81 (0.459) [p=0.547] | -2.56 (0.575) [p=0.257] | -2.55  (0.649) [p=0.459] |
| Olanzapine (n=20) | 5  (0.293) [p=0.573] [[p=0.573]] | -0.59 (0.304) [p=0.552] [[p=0.576]] | -1.67 (0.312) [p=0.272] [[p=0.502]] | -1.85 (0.318) [p=0.167] [[p=0.346]] | -1.48 (0.319) **[p=0.001]** [[p=0.068]] | -1.37 (0.379) **[p=0.003]** **[[p=0.021]]** | -1.76 (0.344) **[p=0.004]** [[p=0.247]] | -1.81  (0.354) **[p=0.025]** [[p=0.33]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S8-6

PANSS P3 for each medication, participants with P3 ≥4, AP+, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Amisulpride (n=24) | 5  (0.281) | -0.96 (0.286) | -2.22 (0.286) | -2.14 (0.304) | -2.53 (0.299) | -2.8 (0.329) | -2.92 (0.315) | -2.55 (0.337) |
| Aripiprazole (n=11) | 4.73 (0.415) [p=0.589] | -0.57 (0.445) [p=0.476] | -1.4 (0.446) [p=0.132] | -2.76 (0.431) [p=0.249] | -3.12 (0.552) [p=0.353] | -2.25 (0.602) [p=0.433] | -1.11 (0.805) **[p=0.038]** | -2.74 (1.094) [p=0.869] |
| Olanzapine (n=14) | 4.79 (0.368) [p=0.646] [[p=0.646]] | -0.54 (0.377) [p=0.384] [[p=0.952]] | -1.16  (0.4) **[p=0.037]** [[p=0.697]] | -1.81 (0.414) [p=0.531] [[p=0.119]] | -1.32 (0.414) **[p=0.021]** **[[p=0.01]]** | -1.25 (0.533) **[p=0.015]** [[p=0.217]] | -1.84 (0.47) [p=0.061] [[p=0.435]] | -1.98  (0.47) [p=0.332] [[p=0.526]] |

Numbers in the baseline column gives the estimated values; numbers in the following columns gives the estimated decrease in PANSS P3 at each visit compared to baseline; Numbers in parentheses are estimated standard deviations (SD); p values in single brackets corresponds to comparison to the reference drug amisulprid; values in double brackets corresponds to comparison to aripiprazole

Table S8-7

PANSS P3 for Olanzapine, participants with P3 ≥4, ITT analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Not naive (n=20) | 5  (0.316) | -0.59 (0.325) | -1.69 (0.332) | -1.85 (0.338) | -1.49 (0.339) | -1.39 (0.393) | -1.77 (0.361) | -1.81  (0.37) |
| Naive (n=10) | 4.9  (0.446) [p=0.856] | -1.6 (0.446) [p=0.06] | -1.47 (0.46) [p=0.697] | -1.32 (0.524) [p=0.385] | -2.1 (0.499) [p=0.299] | -2.68 (0.523) **[p=0.044]** | -2.99 (0.524) **[p=0.05]** | -2.38 (0.499) [p=0.348] |

AP+ participants exposed to antipsychotic treatment before entering the study; AP- no previous exposure to antipsychotic drugs (antipsychotic naïve); Numbers in the baseline column gives the estimated values; numbers in the other columns gives the estimated decrease in PANSS P3 compared to baseline; Numbers in parentheses are estimated standard deviations (SD); Numbers in brackets are p values.

Table S8-8

PANSS P3 for Olanzapine, participants with P3 ≥4, PP analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 1 week | 3 weeks | 6 weeks | 12 weeks | 26 weeks | 39 weeks | 52 weeks |
| Not naive (n=14) | 4.79 (0.372) | -0.54 (0.38) | -1.17 (0.402) | -1.81 (0.414) | -1.32 (0.415) | -1.26 (0.527) | -1.84 (0.467) | -1.99 (0.467) |
| Naive (n=9) | 5  (0.464) [p=0.722] | -1.67 (0.464) [p=0.056] | -1.75 (0.479) [p=0.341] | -1.66 (0.5) [p=0.816] | -2.58 (0.481) **[p=0.046]** | -2.82 (0.499) **[p=0.031]** | -3.38 (0.5) **[p=0.024]** | -2.83 (0.481) [p=0.204] |

AP+ participants exposed to antipsychotic treatment before entering the study; AP- no previous exposure to antipsychotic drugs (antipsychotic naïve); Numbers in the baseline column gives the estimated values; numbers in the other columns gives the estimated decrease in PANSS P3 compared to baseline; Numbers in parentheses are estimated standard deviations (SD); Numbers in brackets are p values.