**SUPPLEMENTARY TABLE S1. Overview of AEs (by lead-in treatment)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Status before enrollment** | **Inpatient treatment in  12-week efficacy study** | |  | **Inpatient treatment in**  **12-week efficacy study** | | **Stable outpatient**  **(*de novo*)** | **Total**  **N = 478** |
| **Placebo**  **(3 doses)**  **n = 29** | **AL 441 mg**  **(3 doses)**  **n = 81** |  | **Placebo**  **(3 doses)**  **n = 26** | **AL 882 mg**  **(3 doses)**  **n = 100** | **Oral antipsychotics**  **n = 24)** |
| **Dosage** | **AL 441 mg q4wk**  **N = 110** | |  | **AL 882 mg q4wk**  **N = 368** | | |  |
| Any AE | 15 (51.7) | 36 (44.4) |  | 14 (53.8) | 44 (44.0) | 132 (54.5) | 241 (50.4) |
| Any drug-related AE | 9 (31.0) | 20 (24.7) |  | 9 (34.6) | 27 (27.0) | 76 (31.4) | 141 (29.5) |
| AE by severity | | | | | | | |
| Mild | 13 (44.8) | 24 (29.6) |  | 5 (19.2) | 24 (24.0) | 71 (29.3) | 137 (28.7) |
| Moderate | 1 (3.4) | 11 (13.6) |  | 7 (26.9) | 17 (17.0) | 51 (21.1) | 87 (18.2) |
| Severe | 1 (3.4) | 1 (1.2) |  | 2 (7.7) | 3 (3.0) | 10 (4.1) | 17 (3.6) |
| Any SAE | 0 | 0 |  | 3 (11.5) | 3 (3.0) | 9 (3.7) | 15 (3.1) |
| Any SAE leading to  discontinuation | 0 | 0 |  | 2 (7.7) | 2 (2.0) | 6 (2.5) | 10 (2.1) |
| Any SAE leading to death | 0 | 0 |  | 0 | 1 (1.0) | 1 (0.4) | 2 (0.4) |
| Any drug-related SAE | 0 | 0 |  | 0 | 0 | 3 (1.2) | 3 (0.6) |
| Any AE leading to  discontinuation | 0 | 1 (1.2)a |  | 3 (11.5) | 5 (5.0) | 19 (7.9) | 28 (5.9) |
| AEs in ≥2% of all patientsa | | | | | | | |
| Insomnia | 1 (3.4) | 2 (2.5) |  | 3 (11.5) | 9 (9.0) | 25 (10.3) | 40 (8.4) |
| Weight increased | 1 (3.4) | 6 (7.4) |  | 4 (15.4) | 4 (4.0) | 9 (3.7) | 24 (5.0) |
| Anxiety | 0 | 4 (4.9) |  | 2 (7.7) | 3 (3.0) | 12 (5.0) | 21 (4.4) |
| Injection site pain | 0 | 1 (1.2) |  | 0 | 1 (1.0) | 16 (6.6) | 18 (3.8) |
| Akathisia | 1 (3.4) | 0 |  | 2 (7.7) | 3 (3.0) | 12 (5.0) | 18 (3.8) |
| Headache | 1 (3.4) | 6 (7.4) |  | 1 (3.8) | 4 (4.0) | 6 (2.5) | 18 (3.8) |
| Schizophrenia | 1 (3.4) | 3 (3.7) |  | 1 (3.8) | 4 (4.0) | 7 (2.9) | 16 (3.3) |
| Nasopharyngitis | 0 | 4 (4.9) |  | 2 (7.7) | 2 (2.0) | 6 (2.5) | 14 (2.9) |
| Weight decreased | 0 | 3 (3.7) |  | 1 (3.8) | 2 (2.0) | 6 (2.5) | 12 (2.5) |
| Tremor | 1 (3.4) | 0 |  | 0 | 4 (4.0) | 7 (2.9) | 12 (2.5) |

AE, adverse event; AL, aripiprazole lauroxil; q4wk, every 4 weeks; SAE, serious adverse event.

aOne patient who discontinued because of weight gain was not included because the AE occurred before the first injection in the long-term study.

**SUPPLEMENTARY TABLE S2. EPS-associated AEs by lead-in treatment**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | ***De novo*a**  **N = 242** | **Prior active ALb**  **N = 181** | **Prior placeboc**  **N = 55** | **Total**  **(N = 478)** |
| Any EPS AE | 29 (12.0) | 10 (5.5) | 6 (10.9) | 45 (9.4) |
| Akathisia | 12 (5.0) | 3 (1.7) | 3 (5.5) | 18 (3.8) |
| Akathisia | 12 (5.0) | 3 (1.7) | 3 (5.5) | 18 (3.8) |
| Restlessness | 2 (0.8) | 0 | 0 | 2 (0.4) |
| Restlessness | 2 (0.8) | 0 | 0 | 2 (0.4) |
| Dyskinesia | 2 (0.8) | 0 | 0 | 2 (0.4) |
| Tardive dyskinesia | 2 (0.8) | 0 | 0 | 2 (0.4) |
| Dystonia | 5 (2.1) | 2 (1.1) | 1 (1.8) | 8 (1.7) |
| Dystonia | 4 (1.7) | 1 (0.6) | 0 | 5 (1.0) |
| Muscle spasms | 1 (0.4) | 1 (0.6) | 0 | 2 (0.4) |
| Oculogyric crisis | 0 | 0 | 1 (1.8) | 1 (0.2) |
| Parkinson-like events | 12 (5.0) | 7 (3.9) | 3 (5.5) | 22 (4.6) |
| Tremor | 7 (2.9) | 4 (2.2) | 1 (1.8) | 12 (2.5) |
| Extrapyramidal disorder | 3 (1.2) | 0 | 1 (1.8) | 4 (0.8) |
| Parkinsonism | 1 (0.4) | 3 (1.7) | 0 | 4 (0.8) |
| Drooling | 1 (0.4) | 0 | 0 | 1 (0.2) |
| Dysphonia | 0 | 0 | 1 (1.8) | 1 (0.2) |

AE, adverse event; AL, aripiprazole lauroxil; EPS, extrapyramidal symptoms.

aFirst injection in the long-term study was the first exposure to AL (882 mg).

bPreviously received three injections of AL in the acute-phase study; the first injection in the long-term study was the fourth exposure to AL (441 or 882 mg).

cPreviously received three injections of placebo in the acute-phase study; the first injection in the long-term study was the first exposure to AL (441 or 882 mg).

**SUPPLEMENTARY TABLE S3. Patients with potentially clinically significant values for metabolic parameters and prolactin at any postbaseline visit**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Criteria** | **AL 441 mg q4wk**  **N = 110**  **n/m (%)** | **AL 882 mg q4wk**  **N = 368**  **n/m (%)** | **Total**  **N = 468**  **n/m (%)** |
| Cholesterol | >300 mg/dL | 2/105 (1.9) | 4/351 (1.1) | 6/456 (1.3) |
| Total cholesterol fasting | ≥240 mg/dL | 18/95(18.9) | 30/306 (9.8) | 48/401 (12.0) |
| HDL cholesterol fasting | ≤30 mg/dL | 9/98 (9.2) | 21/335 (6.3) | 30/433 (6.9) |
| LDL cholesterol fasting | ≥160 mg/dL | 19/100 (19) | 29/311 (9.3) | 48/411 (11.7) |
| Triglycerides fasting | Male ≥160 mg/dL  Female ≥120 mg/dL | 26/62 (41.9) | 81/235 (34.5) | 107/297 (36.0) |
| Glucose low | <50 mg/dL | 1/108 (0.9) | 0/348 | 1/456 (0.2) |
| Glucose high | ≥200 mg/dL | 2/208 (1.0) | 7/348 (2.0) | 9/456 (2.0) |
| Prolactin  Male  Female | ≥1× ULN  ≥2× ULN  ≥3× ULN  ≥1× ULN  ≥2× ULN  ≥3× ULN | 1/32 (3.1)  1/32 (3.1)  0/32  2/21 (9.5)  1/21 (4.8)  0/21 | 6/119 (5.0)  2/119 (1.7)  0/119  12/89 (13.5)  4/89 (4.5)  2/89 (2.2) | 7/151 (4.6)  3/151 (2.0)  0/151  14/110 (12.7)  5/110 (4.5)  2/110 (1.8) |

AL, aripiprazole lauroxil; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PCS, potentially clinically significant; q4wk, every 4 weeks; ULN, upper limit of normal.

m is the number of patients with non-PCS values at baseline and at least one postbaseline assessment.