Synopsis – Study 14724A

Title of Study A 28-week, randomised, open-label study evaluating the effectiveness of aripiprazole once-monthly *versus* paliperidone palmitate in adult patients with schizophrenia
Investigators 71 investigators at 71 centres in 10 countries Signatory investigator – [redacted]
Study Centres 71 centres – 6 in Canada, 9 in Czech Republic, 2 in Estonia, 6 in France, 9 in Germany, 10 in Italy, 9 in Spain, 3 in Sweden, 1 in United Kingdom, and 16 in United States
Publications None (as of the date of this report)
Study Period *First patient first visit* – 28 February 2013 *Last patient last visit* – 29 September 2014
Objectives • *Primary objective:* – to demonstrate that the effectiveness of aripiprazole once-monthly (400 or 300 mg/month) was non-inferior to that of paliperidone intramuscular (IM) injection (50 to 150 mg/month Xeplion®[European Union]/ Invega® Sustenna® [Canada] or 78 to 234 mg/month Invega® Sustenna® [United States]) in adult patients with schizophrenia • *Secondary objectives*: – To compare the effectiveness of aripiprazole once-monthly *versus* paliperidone palmitate on: • clinical global impression • time to all-cause withdrawal • response rates • symptomatic remission rate • functional remission rate • subjective treatment satisfaction • quality of life related to tolerability • resource utilisation assessment • *Safety objective:* – to compare the safety and tolerability of aripiprazole once-monthly *versus* paliperidone palmitate in adult patients with schizophrenia

Methodology

- This was an interventional, multi-national, multi-site, randomised, open-label, rater-blinded, parallel-group, active-comparator (paliperidone palmitate), flexible-dose study.
- The patients were randomised equally (1:1) to aripiprazole oral tablets followed by monthly IM injections of aripiprazole once-monthly or paliperidone oral tablets followed by monthly IM injections of paliperidone palmitate. Patients were stratified according to age (2 strata: patients ≤35 and >35 years of age) and equally distributed between the treatment groups.
- The patients randomised to aripiprazole received 5 to 30 mg/day of oral aripiprazole during the 3-week Oral Conversion Period (Period A). During the 5-week IM Treatment Initiation Period (Period B), patients received 1 week of oral aripiprazole prior to initiation of 400 mg IM aripiprazole on Day 28. The initiation of IM aripiprazole was followed by 14 consecutive days of concurrent treatment with oral aripiprazole 10 to 20 mg/day. During the IM Treatment Continuation Period (Period C), the patients randomised to aripiprazole received 400 mg or 300 mg/month of IM aripiprazole for 20 weeks.
- The patients randomised to paliperidone received 3 to 12 mg/day of oral paliperidone during the 3-week Oral Conversion Period (Period A). During the 5-week IM Treatment Initiation Period (Period B), the patients randomised to paliperidone received 150 mg Xeplion® (European Union)/Invega® Sustenna® (Canada) or 234 mg Invega® Sustenna® (United States) on Day 21, followed by a 100 mg or 156 mg dose, respectively, on Day 28. During the IM Treatment Continuation Period (Period C), the patients randomised to paliperidone received 50 to 150 mg Xeplion®/Invega® Sustenna® (European Union/Canada)or 78 to 234 mg Invega® Sustenna® (United States) for 20 weeks.
- The study visits were performed at 1-week intervals between Weeks 2 and 4 of treatment and then every 4 weeks until the end of the 28-week treatment period.
- A safety follow-up visit was scheduled for 4 weeks after completion of the study or after withdrawal from the study (except for patients who received aripiprazole once-monthly and who were included in the extension study, Study 14724B).

Number of Patients Planned and Analysed

- A total of 286 patients were planned for enrolment: 143 in the aripiprazole group and 143 in the paliperidone group.
- Patient disposition is tabulated below:

	Aripiprazole		Paliperidone		Total	
	n	(%)	n	(%)	n	(%)
Patients randomised	148		147		295	
Patients treated (all-patients-treated set [APTS]):	144	97.3	137	93.2	281	95.3
Patients completed	100	67.6	83	56.5	183	62.0
Patients withdrawn	44	29.7	54	36.7	98	33.2
Primary reason for withdrawal:						
Adverse event(s)	16	11.1	27	19.7	43	15.3
Lack of efficacy	8	5.6	3	2.2	11	3.9
Non-compliance with IMP	1	0.7	1	0.7	2	0.7
Protocol violation	6	4.2	4	2.9	10	3.6
Withdrawal of consent	7	4.9	12	8.8	19	6.8
Lost to follow-up	2	1.4	5	3.6	7	2.5
Other	4	2.8	1	0.7	5	1.8
Analysis sets:						
All-patients-randomised set (APRS)	148		147		295	
APTS	144	97.3	137	93.2	281	95.3
Full-analysis set (FAS)	136	91.9	132	89.8	268	90.8
Per-protocol set (PPS)	122	82.4	112	76.2	234	79.3

Diagnosis and Main Inclusion Criteria

Outpatients with a primary diagnosis of schizophrenia according to DSM-IV-TR™ criteria, who:

- had a Clinical Global Impression – Severity of Illness (CGI-S) score ≥3 (mildly ill) and ≤5 (markedly ill) at the Screening and at Baseline Visits
- were between 18 and 60 years of age (extremes included); it was the intention that at least one-third of the patients were ≤35 years of age
- were prescribed antipsychotic treatment for the full 3 months prior to the Screening Visit
- were in need of a change in the current antipsychotic treatment and in the judgement of the investigator could benefit from an extended treatment with a once-monthly formulation, including but not limited to any of the following reasons:
  - lack of adequate response to their current antipsychotic medication
  - poor tolerability to their current antipsychotic medication
  - lack of adherence to their current antipsychotic medication

Investigational Medicinal Product, Doses and Modes of Administration, Batch Numbers

Aripiprazole– 5, 10, and 15 mg/day, tablets, orally; Batch Nos. P1492, P1493, P1494, P1503, P1504, P1505, P1567, P1568, P1604, P1605, and P1606

Aripiprazole once-monthly – 400 and 300 mg/4 weeks, IM injection; Batch Nos. P1509 and P1498

Duration of Treatment

28 weeks (3-week oral conversion [Period A], 5-week IM treatment initiation [Period B], and 20-week IM treatment continuation [Period C]) followed by a 4-week safety follow-up period

Reference Therapy, Doses, and Modes of Administration, Batch Numbers

- *Paliperidone* – 3, 6, and 9 mg/day, tablets, orally; batch No. P1495, P1496, P1497, P1506 P1507, P1508, P1569, P1570, P1607, P1608, P1609, and P1619
- *Paliperidone IM injection* – 50, 75, 100, and 150 mg Xeplion® (European Union)/Invega® Sustenna® (Canada)or 78, 117, 156, 234 mg Invega® Sustenna® (United States)/4 weeks, IM injection; batch No. P1499, P1500, P1501, P1502, P1510, P1511, P1512, P1513, P1610, P1611, P1612, P1613, P1571, P1572, P1573, and P1574

Effectiveness Assessments

- Quality of Life Scale (QLS) to measure the primary endpoint
- Investigator's Assessment Questionnaire (IAQ)
- Clinical Global Impression – Severity of Illness (CGI-S)
- Clinical Global Impression – Global Improvement (CGI-I)
- Subjective Well-being under Neuroleptics - short version (SWN-S)
- Tolerability and Quality of Life (TooL)
- Arizona Sexual Experience Scale (ASEX)
- The Readiness for Work Questionnaire (WoRQ)

Pharmacoeconomic Assessments

- Health Economic Assessments (HEA)

Safety Assessments

- Adverse events (AEs), clinical safety laboratory tests, vital signs, weight/body mass index (BMI), waist circumference, electrocardiograms (ECGs), physical and neurological examinations, and Columbia-Suicide Severity Rating Scale (C-SSRS) assessments

Statistical Methodology

- The following analysis sets were used to analyse and present the data:
- *all patients-randomised set* (APRS) - all randomised patients
- *all patients-treated set* (APTS) - all randomised patients who took at least 1 dose of oral IMP
- *full-analysis set* (FAS) - all patients in the APTS who had both a valid baseline assessment and at least 1 valid post-baseline assessment of the QLS total score
- *per-protocol set* (PPS) - all patients in the FAS who did not use disallowed concomitant medication judged to interfere with the treatment response during the treatment period; had at least 1 injection of the IMP formulation; and were rated on QLS and IAQ by a blinded rater
- The effectiveness analyses were based on the FAS. For the primary analysis of the primary endpoint (change from baseline to Week 28 in QLS total score), comparisons of aripiprazole once-monthly *versus* paliperidone palmitate were made using estimates from a mixed model for repeated measurements (MMRM) using an unstructured covariance matrix. The model included baseline QLS total score-by-visit interaction, geographical region (Europe yes/no), age group (age ≤35 years yes/no), visit, and treatment-by-visit interaction as fixed effects. Non-inferiority was considered confirmed if the lower bound of the 2-sided 95% confidence interval (CI) was > -5, or equivalently, if the p-value for the 1-sided test of
$$H_0: D \leq -5 \text{ against } H_1: D > -5$$
was less than or equal to 2.5%, where D was the mean treatment difference (aripiprazole minus paliperidone). If non-inferiority was confirmed, then superiority of aripiprazole over paliperidone was investigated. Superiority was considered confirmed if the lower bound of the two-sided 95% CI was > 0.
- To check for robustness of the result for FAS, the primary analysis of effectiveness was repeated for the PPS. Sensitivity analyses of the primary endpoint were performed using an analysis of covariance (ANCOVA) for observed cases (OC) and last observation carried forward (LOCF) with treatment and geographical region as fixed factors and the baseline score as a covariate (the study included sites from 2 geographical regions: Europe and United States/Canada.
- For continuous secondary endpoints (IAQ total score, change from baseline in CGI-S, change from baseline in the QLS domain scores, SWN-S total score, and TooL total score), the same methodology as that described for the primary endpoint was used. The analyses of other endpoints are summarised below:
  - An analysis of CGI-I scores was first performed using a parametric approach (MMRM including baseline CGI-S as an explanatory variable) and next using a non-parametric approach: at Week 28, a non-parametric test (Wilcoxon) was used to compare treatment groups.
  - The proportion of responders (response yes/no, a binary variable) for CGI-S, was compared, where response was defined as a CGI-S score of ≤2 at Week 28, as well as at Week 16. A logistic regression model was used with treatment, age group, and region as factors and baseline CGI-S as a covariate.
  - For ASEX, the total score and the 5 items were analysed by descriptive methods. In addition, an analysis was performed on the patients who presented with sexual dysfunction on the ASEX scale.
  - The proportion of patients in symptomatic remission (CGI-S ≤3, or CGI-S=4 with an improvement of at least 2 points from baseline) at Week 28 and Week 16, as well as at any visit, were analysed using a logistic regression model with treatment, age group, and region as factors and baseline CGI-S as a covariate.
  - Successful Treatment Time was defined as the number of months of treatment in which the criterion for symptomatic remission was fulfilled, and was presented descriptively. For each visit the criterion was fulfilled, the time to next visit was adjudicated to the time. In cases where the next visit was missing, the planned number of days to next visit was used.
  - The proportion of patients in functional remission (QLS total score change from baseline ≥10 points) at Week 28 and Week 16, as well as at any visit, was analysed using a logistic regression model with treatment, age group, and region as factors and baseline QLS total score as a covariate.
  - Survival analysis of time to all-cause withdrawal from baseline was analysed. Survival curves of Kaplan-Meier type were produced. A log-rank test was applied to compare the treatment groups. In addition, a comparison in median time to withdrawal was also done using Hodges-Lehmann estimation.

Statistical Methodology (continued)

- All effectiveness analyses were repeated on the strata of patients aged ≤35 years and >35 years.
- The proportion of patients receiving concomitant CNS medications, and proportion of patients receiving anticholinergic medications for EPS at any time during the study were analysed descriptively.
- The change from baseline to Week 28 in the WoRQ total score was to be analysed using an ANCOVA model, with treatment, age group and region as factors and the baseline score as a covariate. In addition, a shift analysis on the WoRQ readiness to work question was summarised.

- For IAQ, which was not assessed at baseline, the baseline QLS score was included as an explanatory variable in the model.
- The safety analyses were based on the APTS. Adverse events, clinical safety laboratory tests, vital signs, ECGs, and anthropometric measures were summarised using descriptive statistics. In addition, AE summaries were split by treatment period (Periods A, B, and C and Safety Follow-up).

Demography of Study Population

- The mean age was approximately 42 years.
- Men comprised 60% of the study population.
- Most of the patients were White (70%) and 27% of patients were Black.
- At baseline, the mean BMI was 30 kg/m^2 and the mean waist circumference was 98 cm.
- At baseline, the BMI classification for 41% of patients was obese, 36% were overweight, and 23% were of normal weight.
- All the demographic characteristics for the aripiprazole and paliperidone treatment groups were comparable at baseline.
- At baseline the mean QLS total score was 66 points for the aripiprazole group and 63 points for the paliperidone group. No relevant differences between the aripiprazole and paliperidone groups were observed for the mean QLS subscale scores at baseline.
- The mean CGI-S score at baseline was 4.0 points for both treatment groups.
- The mean SWN-S total scores were 84 and 85 points for the aripiprazole and paliperidone groups, respectively; no relevant differences between the treatment groups were observed in the SWN-S subscale scores.
- The mean TooL total score was 14 points for both treatment groups and there were no relevant differences between the treatment groups in TooL domain scores.
- No relevant differences between the treatment groups were observed in mean values for ASEX total score, ASEX item scores, or WoRQ total score at baseline.

Effectiveness Results

- Non-inferiority of aripiprazole treatment at Week 28 was established, as the lower bound of the 95% CI of the mean difference for the aripiprazole and paliperidone comparison was 0.3 QLS points, and therefore above the non-inferiority criterion of -5 QLS points. In addition, superiority of aripiprazole treatment at Week 28 was established, as the lower bound of the 95% CI was >0. Therefore, the primary objective of the study was met.
- The mean improvement from baseline in QLS total score at Week 28 based on the MMRM using the FAS were 7.5 and 2.8 points in the aripiprazole and the paliperidone groups, respectively, giving a statistically significant mean difference of 4.7 points in favour of aripiprazole (95% CI: 0.32, 9.02; p = 0.036).

Effectiveness Results (continued)

- The MMRM based on the PPS confirmed the non-inferiority of aripiprazole treatment at Week 28; the lower bound of the 95% CI was -0.5 (mean difference: 3.9 QLS points in favour of aripiprazole treatment; the upper bound of the 95% CI was 8.29).
- In addition, the primary effectiveness analysis was assessed using an ANCOVA based on the FAS using LOCF and OC, both of which supported the effectiveness of aripiprazole treatment versus paliperidone treatment.
- The mean IAQ total scores at Week 28 based on the MMRM using the FAS were 32.3 and 33.8 points in the aripiprazole and paliperidone groups, respectively, giving a statistically significant mean difference of -1.5 points in favour of aripiprazole (95% CI: -2.94 to 0.05; p = 0.043).
- The mean changes from baseline in CGI-S scores at Week 28 based on the MMRM using the FAS were -0.8 and -0.5 points in the aripiprazole and paliperidone groups, respectively, giving a statistically significant mean difference of -0.3 points in favour of aripiprazole (95% CI: -0.48 to -0.09; p = 0.004).
- The mean improvement from baseline in the intrapsychic foundations QLS subscale score at Week 28 based on the MMRM using the FAS were 2.3 and 0.5 points in the aripiprazole and paliperidone groups, respectively, giving a statistically significant mean difference of 1.8 points in favour of aripiprazole (95% CI: 0.09 to 3.41; p = 0.039). Numerically greater mean increases from baseline in other QLS subscale scores were observed in the aripiprazole group *versus* the paliperidone group at Week 28; however, the differences were not statistically significant.
- The mean improvement from baseline in SWN-S total score at Week 28 based on the MMRM using the FAS were 4.8 and 3.8 points in the aripiprazole and paliperidone groups, respectively, giving a mean non-statistically significant difference of 1.0 points in favour of aripiprazole (95% CI: -2.40 to 4.42; p = 0.561).
- The mean changes from baseline in TooL total scores at Week 28 based on the MMRM using the FAS were -1.7 and -1.1 points in the aripiprazole and paliperidone groups, respectively, giving a mean non-statistically significant difference of -0.7 points in favour of aripiprazole (95% CI: -1.51 to 0.12; p = 0.095).
- The proportion of patients having sexual dysfunction was numerically lower in the aripiprazole group *versus* the paliperidone group at Week 28 (61% *versus* 67%; 95% CI for odds ratio: 0.48 to 1.32; FAS).
- The mean CGI-I score at Week 28 based on the MMRM using the FAS were 2.7 and 3.1 points in the aripiprazole and paliperidone groups, respectively, giving a statistically significant mean difference of -0.3 points in favour of aripiprazole (95% CI: -0.60 to -0.05; p = 0.020).
- Comparable proportions of CGI-S responders were observed in the aripiprazole and paliperidone groups at Week 28 (12% *versus* 9%; 95% CI for odds ratio: 0.50 to 3.51; p = 0.563; FAS, logistic regression) and Week 16 (10% *versus* 8%; 95% CI for odds ratio: 0.45 to 3.17; p = 0.723; FAS, logistic regression).
- The proportion of symptomatic remitters was statistically significantly greater in the aripiprazole group *versus* the paliperidone group at Week 28 (66% *versus* 47%; 95% CI: 1.43 to 5.71; p = 0.003; FAS, logistic regression). A comparable symptomatic remission rate was observed in the aripiprazole and paliperidone groups at Week 16 (54% *versus* 43%; 95% CI for odds ratio: 0.93 to 3.19; p = 0.068; logistic regression) and at any time point (66% *versus* 58%; 95% CI for odds ratio: 0.97 to 3.09; p = 0.062; logistic regression).
- A comparable functional remission rate was observed in the aripiprazole and paliperidone groups at Week 28 (41% *versus* 37%; 95% CI for odds ratio: 0.69 to 2.30; p = 0.454; logistic regression), Week 16 (34% *versus* 28%; 95% CI for odds ratio: 0.85 to 2.85; p = 0.156; logistic regression), and at any week (47% *versus* 37%; 95% CI for odds ratio: 0.92 to 2.49; p = 0.101; logistic regression).
- The Kaplan-Meier plot to time to discontinuation showed a numerically lower incidence of all-cause discontinuation with aripiprazole than with paliperidone and a longer time to discontinuation in the aripiprazole group (p = 0.076).
- The mean IAQ negative symptoms, weight gain, and EPS (other than akathisia) item scores at Week 28 based on the MMRM using the FAS were 2.3 and 2.6, 2.9 and 3.1, and 2.8 and 3.0 points in the aripiprazole and paliperidone groups, respectively, giving statistically significant mean differences of -0.3, -0.3, and -0.2 points, respectively, in favour of aripiprazole (95% CI: -0.59 to 0.08; p = 0.010; -0.49 to 0.02; p = 0.034; and -0.31 to 0.01; p = 0.014, respectively).

Effectiveness Results (continued)

- The mean improvement from baseline in SWN-S mental functioning, physical functioning, and self-control subscores at Week 28 based on the MMRM using the FAS were 1.3 and 0.7, 0.8 and 0.2, and 1.4 and 0.9 points, respectively, in the aripiprazole and paliperidone groups, respectively, giving a mean non-statistically significant difference of 0.5, 0.5, and 0.6 points, respectively, in favour of aripiprazole (95% CI: -0.42 to 1.50, -0.44 to 1.49, and -0.34 to 1.44; p = 0.265, 0.286, and 0.223, respectively). There were no statistically significant differences between the treatment groups at Week 28 in the SWN-S emotional regulation or social integration subscores.
- Based on the MMRM using the FAS, the mean improvements from baseline to Week 28 for 7 of the 8 TooL domain scores were numerically greater in the aripiprazole group *versus* the paliperidone group.
- The mean improvement from baseline in QLS total score at Week 16 based on the MMRM using the FAS were 5.5 and 1.9 points in the aripiprazole and the paliperidone groups, respectively, giving a statistically significant mean difference of 3.6 points in favour of aripiprazole (95% CI: 0.025, 7.26; p = 0.048. The mean changes from baseline in CGI-S scores at Week 16 based on the MMRM using the FAS were -0.6 and -0.4 points in the aripiprazole and paliperidone groups, respectively, giving a mean difference of -0.2 points in favour of aripiprazole (95% CI: -0.39 to 0.002; p = 0.052). The mean improvement from baseline in SWN-S total scores at Week 16 based on the MMRM using the FAS were 5.4 and 2.5 points in the aripiprazole and paliperidone groups, respectively, giving a mean non-statistically significant difference of 2.9 points in favour of aripiprazole (95% CI: -0.58 to 6.36; p = 0.102).
- The mean change from baseline in WoRQ total score at Week 28 based on the ANCOVA using the FAS were -1.7 and -0.7 points in the aripiprazole and paliperidone groups, respectively, giving a statistically significant mean difference of -1.2 points in favour of aripiprazole (95% CI: -1.96 to -0.37; p = 0.004).
- In general, resource consumption decreased from baseline to Week 28/withdrawal and was similar between the treatment groups.
- Analyses of the effectiveness variables by age strata were generally consistent with the corresponding analyses for the FAS with apparent larger effects observed in patients ≤35 years of age.

Safety Results

- The AE incidence for all study periods is summarised below:

	Aripiprazole		Paliperidone	
	n	(%)	n	(%)
Patients treated	144		137	
Patients who died	0		0	
Patients with treatment-emergent serious AEs (SAEs)	12	8.3	10	7.3
Patients with TEAEs leading to withdrawal	17	11.8	28	20.4
Patients with TEAEs	97	67.4	101	73.7
Total number of AEs	284		352	

Safety Results (continued)

- The most frequently-occurring AEs in all study periods are summarised below (>5% in any treatment group):

Preferred Term (MedDRA Version 16.1)	Aripiprazole n (%)	Paliperidone
All study periods (number of patients treated):	144	137
Patients with any TEAE	97 (67.4%)	101 (73.7%)
Accidental overdose	30 (20.8%)	13 (9.5%)
Insomnia	17 (11.8%)	17 (12.4%)
Weight increased	13 (9.0%)	19 (13.9%)
Anxiety	8 (5.6%)	12 (8.8%)
Dizziness	5 (3.5%)	12 (8.8%)
Somnolence	9 (6.3%)	8 (5.8%)
Injection site pain	4 (2.8%)	11 (8.0%)
Akathisia	8 (5.6%)	6 (4.4%)
Headache	3 (2.1%)	11 (8.0%)
Nasopharyngitis	6 (4.2%)	8 (5.8%)
Fatigue	4 (2.8%)	7 (5.1%)
Nausea	3 (2.1%)	8 (5.8%)

- The safety and tolerability profile exhibited for patients treated with aripiprazole once-monthly during this study was consistent with the known characteristics of aripiprazole.
- For all study periods combined, the proportion of patients with TEAEs leading to study withdrawal was lower for the aripiprazole group compared with the paliperidone group. The proportions of patients with treatment-emergent SAEs were comparable between the treatment groups. No deaths or pregnancies occurred during the study.
- For all study periods combined, TEAEs of *accidental overdose* occurred in a greater proportion of patients in the aripiprazole group (21%) compared with the paliperidone group (10%). *Accidental overdose* occurred in similar proportions for both treatment groups during the oral conversion period, but in a greater proportion for the aripiprazole group during the IM treatment initiation period, as the patients in the aripiprazole group continued with oral aripiprazole 1 week prior to and for 2 weeks following IM initiation, whereas patients in the paliperidone group discontinued oral paliperidone during the IM treatment initiation period. None of the *accidental overdose* events were considered SAEs, led to study withdrawal, or were accompanied by clinically relevant symptoms.
- Otherwise, the proportions of patients with the most frequently-reported TEAEs (≥5%) in the aripiprazole group were lower than or comparable to the proportions for the paliperidone group.
- There was a greater proportion of patients who had treatment-emergent SAEs of schizophrenia in the aripiprazole group compared with the paliperidone group; otherwise, there were no clinically meaningful differences between the treatment groups in the proportions of treatment-emergent SAEs. Most TEAEs during the study were of mild or moderate intensity.
- The proportion of patients with injection site pain in all study periods combined was lower in the aripiprazole group compared with the paliperidone group; otherwise, there were no clinically meaningful differences between the treatment groups in the proportions of injection site reactions.
- Akathisia was the most commonly reported EPS-related TEAE and occurred in similar proportions in the aripiprazole group and the paliperidone group. The numbers of patients with other individual EPS-related symptoms was generally small and there were no apparent clinically meaningful differences between the treatment groups or between the study periods.
- For all study periods combined, there were 6 (2%) patients with prolactin-related TEAEs (including *hyperprolactinaemia* and *blood prolactin increased*), all of which occurred in patients in the paliperidone group.
- Mean prolactin decreased for the aripiprazole group over the duration of the study while mean prolactin in the paliperidone group increased. Otherwise, there were no clinically meaningful differences between the treatment groups in laboratory, vital sign, or ECG parameters.

Safety Results (continued)

- The C-CASA and C-SSRS scores were comparable at baseline for both treatment groups. One patient in the aripiprazole group attempted suicide during the study and 1 patient in the aripiprazole group had self-injurious behaviour without suicidal intent. The proportions of patients with suicidal ideation during the study were low and no clinically meaningful differences between the treatment groups in suicidal ideation were found.

Conclusions

- Treatment with aripiprazole once-monthly (400 or 300 mg/month) showed superior improvements relative to paliperidone IM injection (50 to 150 mg/month Xeplion® or Invega® Sustenna® [European Union and Canada] or 78 to 234 mg/month Invega® Sustenna® [United States]) on health-related quality of life as measured by the clinician-rated QLS in adult patients with schizophrenia, which was confirmed by statistically significant differences in favour of aripiprazole on the 2 key secondary clinician-rated scales, IAQ and CGI-S, as well.
- A favourable tolerability profile, including numerically lower incidences of TEAEs and TEAEs leading to study withdrawal, were observed among patients treated with aripiprazole once-monthly as compared to those treated with paliperidone IM injection. The safety and tolerability profile exhibited during this study was consistent with the known characteristics of aripiprazole.

Date of the Report

20 April 2015

This study was conducted in compliance with the principles of Good Clinical Practice.