CLINICAL STUDY REPORT SYNOPSIS

Name of Sponsor/Company	Janssen Korea
Name of Finished Product	INVEGA®
Name of Active Ingredient(s)	076477 (Paliperidone)

Status: Approved
Date: 17 February 2014
Prepared by: Janssen Korea Medical Affairs

Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

Protocol No.: R076477SCH4064

Title of Study: An open-label, prospective, randomized and comparative study of patient satisfaction between continued administrations of previous antipsychotics versus switched administration to paliperidone ER in non-satisfied schizophrenia patients with previous antipsychotic drug

Study Name: PRESENT

NCT No.: NCT01592201

Clinical Registry No.: CR100782, PAL-KOR-4019 (Local Trial Number)

Coordinating Investigator: Min-Soo Lee. Korea University Medical Center - Korea University Anam Hospital, Seoul, Republic of Korea

Study Centers: Konkuk University Medical Center, Konkuk University Chungju Hospital, Kyungpook National University Hospital, Korea University Anam Hospital, National Health Insurance Service Ilsan Hospital, Dankook University Hospital, Dong-A University Hospital, Kangbuk Samsung Hospital, Soonchunhyang University Hospital Seoul, Eulji General Hospital, Inje University Sanggye Paik Hospital, Eulji University Medical Center, Hallym University Medical Center, Hanyang University Guri Hospital

Publication: NA (Early Terminated)

Study Period: This clinical study was performed between 10 Jul, 2012 (enrollment of the first subject) and 24 Jun, 2013 (final visit of the last subject).

Phase of Development: Phase 4

OBJECTIVES:

Primary objective

The primary objective of this clinical study was to compare the changes in patient satisfaction measured in the 8-week assessment between aggressive treatment with previous antipsychotics, such as dose adjustment and concomitant use of other antipsychotic drugs (control group), versus switched administration to paliperidone ER (treatment group) in schizophrenia patients dissatisfied with previous antipsychotic drugs.

Important secondary objectives

The important secondary objectives of this clinical study were to compare the following measures between treatment and control group:

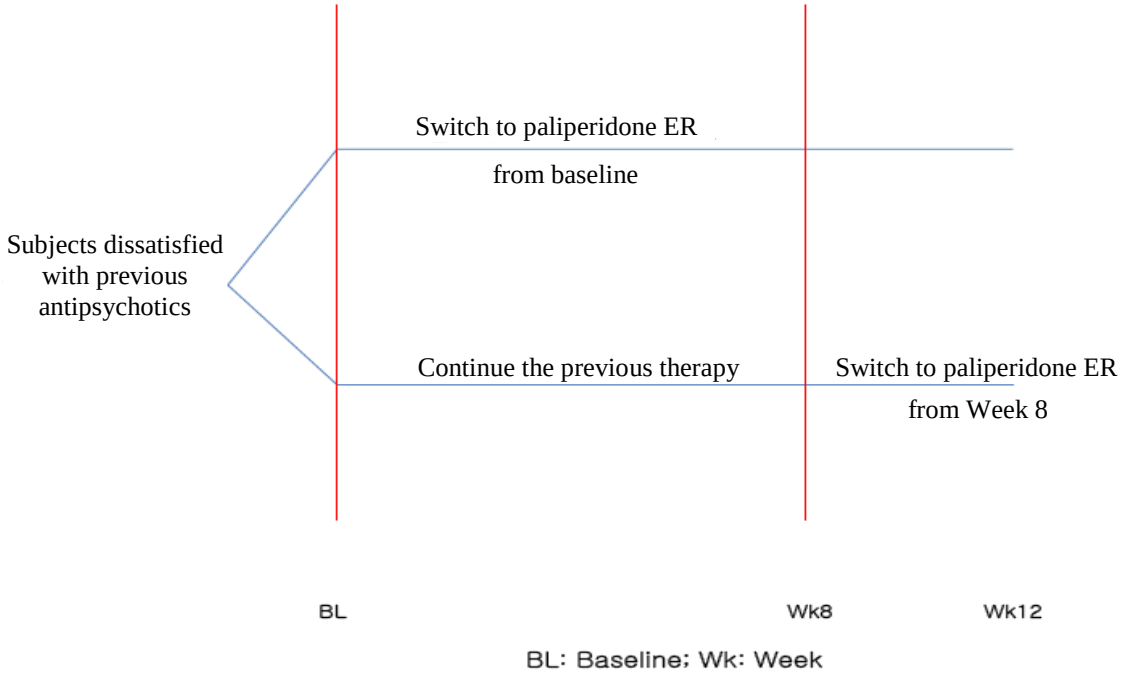
- PANSS : Positive And Negative Symptom Scale
- KDAI-10 : Korean Drug Attitude Inventory
- PSP : Personal and Social Performance Scale
- Sleep VAS : Sleep Visual Analog Scale(Quality of sleep, Daytime drowsiness)

METHODS:

This clinical study is a 12-week, multicenter, open-label, randomized, comparative study, consisting of 14-day (maximum) screening period, 12-week treatment period and study completion/early withdrawal

visits. Schizophrenia patients dissatisfied with previous treatment with risperidone, aripiprazole or olanzapine for at least 6 weeks before screening were randomly assigned to one of two treatment groups. Subjects received treatment immediately switched to paliperidone ER (switching group) or aggressive treatment with previous antipsychotics, such as dose adjustment and concomitant use of other antipsychotic drugs (control group), for 8 weeks. After 8 weeks of treatment period, the control group switched to 4-week paliperidone ER treatment.

The following figure is the chart of study design.



Number of Subjects (planned and analyzed):

Although a total of 402 subjects (201 for each group) were required to test the primary hypothesis of this study, only 13 subjects were randomized to either the switching group (n=8) or the control group (n=5).

Table 1. Data Sets Analyzed: All Subjects Analysis Set

	Switching group n (%)	Control group n (%)	Total n (%)
Planned subjects	201 (100%)	201 (100%)	402 (100%)
Consented subjects			18 (4%)
Randomized subjects	8 (4%)	5 (2%)	13 (3%)
Full Analysis Set population	8 (4%)	5 (2%)	13 (3%)
Safety population	8 (4%)	5 (2%)	13 (3%)

NOTE: Full Analysis Set population includes all randomized subjects.
NOTE: Safety population includes all subjects who received at least 1 dose of study drug.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION:

Key inclusion criteria

- Male or female aged from 20 to 65
- Patients who were diagnosed with schizophrenia according to the DSM-IV criteria

- Subjects who well understood the purpose and procedures of this clinical study and signed the written informed consent
- Patients who have been receiving atypical antipsychotics (risperidone, aripiprazole or olanzapine) as a main treatment for at least 6 weeks before screening
- Patients whose MSQ score was ≤3 before randomization

Key exclusion criteria

- Patients who used paliperidone ER within 3 months before screening
- Patients who used clozapine or other long-acting antipsychotic injections within 3 months before screening
- Patients who have been using two or more different antipsychotics at screening
- Patients with admission histories for 8 consecutive weeks within 6 months before screening

TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, BATCH NO.:

Test Product: Paliperidone ER 3mg, Paliperidone ER 6mg and Paliperidone ER 9mg

Dose and Mode of Administration, Duration of Treatment:

The switching group received paliperidone ER according to the recommended dose and mode of administration for up to 12 weeks at the discretion of clinicians. The control group switched to 4-week paliperidone ER treatment at Week 8.

Lot Numbers:

- Paliperidone ER 3mg 30T: 15668, 16844
- Paliperidone ER 6mg 30T: 15669, 16845
- Paliperidone ER 9mg 30T: 15670, 16751

REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, BATCH NO.:

Test Products: RISPERDAL TAB. 1mg, RISPERDAL TAB. 2mg, RISPERDAL TAB. 3mg, ZYPREXA TAB. 2.5mg, ZYPREXA TAB. 5mg, ZYPREXA TAB. 10mg, ABILIFY TAB. 2mg, ABILIFY TAB. 5mg, ABILIFY TAB. 10mg, ABILIFY TAB. 15mg

Dose and Mode of Administration:

The control group continued the previous therapy (risperidone, aripiprazole or olanzapine) according to the recommended dose and mode of administration for up to 8 weeks at the discretion of clinicians.

Lot Numbers:

- RISPERDAL TAB. 1mg 30T: 15757
- RISPERDAL TAB. 2mg 30T: 15761, 16096
- RISPERDAL TAB. 3mg 30T: 15762, 16909
- ZYPREXA TAB. 2.5mg 28T: A926237, C006897
- ZYPREXA TAB. 5mg 28T: A919161
- ZYPREXA TAB. 10mg 56T: A920566, A963335
- ABILIFY TAB. 2mg 30T: AC11B008, AC124004
- ABILIFY TAB. 5mg 30T: AM119012, AM122003

- ABILIFY TAB. 10mg 30T: AT119004, AT122002
- ABILIFY TAB. 15mg 30T: AF11A006, AF125004

CRITERIA FOR EVALUATION:

Medication Satisfaction Questionnaire (MSQ)

The Medication Satisfaction Questionnaire (MSQ) is a 7-point scale rated as follows: 1=Extremely Dissatisfied, 2=Very Dissatisfied, 3=Somewhat Dissatisfied, 4=Neither Satisfied Nor Dissatisfied, 5=Somewhat Satisfied, 6=Very Satisfied, 7=Extremely Satisfied. A difference of ≥0.5 point (SD, 1.5) in patient satisfaction between the switching and control group at Week 8 from baseline was considered to be significant.

Positive And Negative Symptom Scale (PANSS)

Of the 30 items included in the Positive And Negative Symptom Scale (PANSS), 7 constitute a Positive Scale for measuring productive symptoms, 7 a Negative Scale for measuring deficit features, and the remaining 16 a General Psychopathology Scale. The overall severity of schizophrenia was estimated by total score.

Korean Drug Attitude Inventory (KDAI-10)

The Korean Drug Attitude Inventory (KDAI-10) includes 6 items for subjective positive attitudes and 4 items for subjective negative attitudes toward antipsychotic drugs. A positive response is scored +1 point and a negative one -1 point. Total score is calculated by summing the scores of each item. The total score was used to quantify the subjective responses toward medications for schizophrenia.

Personal and Social Performance (PSP)

The Personal and Social Performance (PSP) is used to measure the extent of difficulties for 1 month expressed by subjects in four main behavior areas: socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behavior. This 100-point rating scale (1 to 100) is divided into 10 levels; 71–100, reflecting mild functioning difficulties; and 0–30, reflecting functioning so poor that the patient needs intensive support and supervision.

Sleep VAS

The Sleep VAS is a measure to assess the quality of sleep and daytime drowsiness. How well the subjects slept for the last 7 days and how sleepy they felt at that time were expressed on 100-mm lines.

STATISTICAL METHODS:

The primary endpoint of this study was the MSQ score. Considering that the difference of ≥0.5 point (SD, 1.5) in patient satisfaction between switching to paliperidone ER and aggressive treatment with the previous antipsychotics was significant, we estimated the mean difference between the switching group ($\mu 1$) and the control ($\mu 2$) as follows:

$$\mu 1_{(\mathrm{MSQ_{Wk\,8}}-\mathrm{MSQ_{Wk\,0}})}-\mu 2_{(\mathrm{MSQ_{Wk\,8}}-\mathrm{MSQ_{Wk\,0}})\geq 0.5}$$

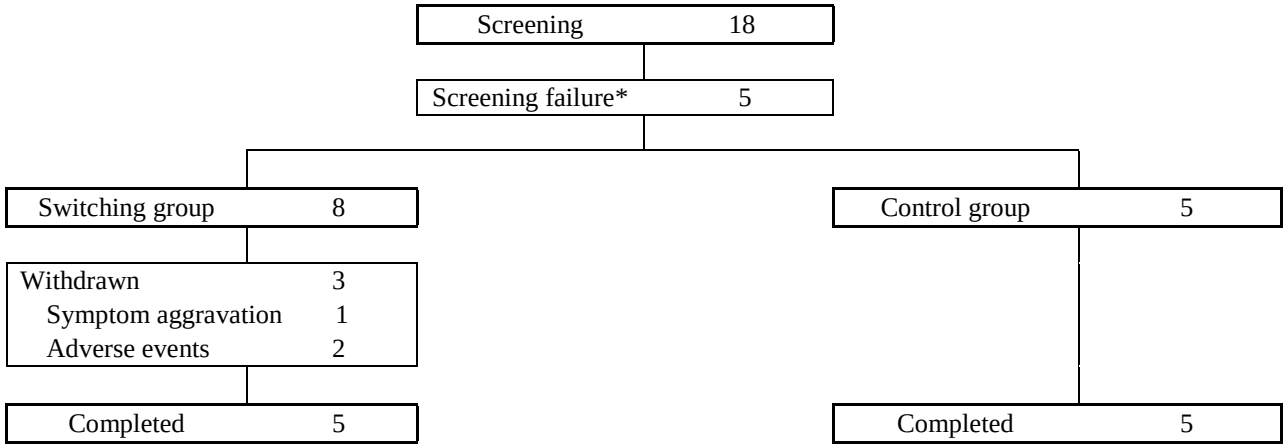
The required number of subjects calculated from a two-sided test at a significance level of 5% with 80% of statistical power was 141 for each group. Allowing for a 30 % withdrawal rate, a total of 402 subjects were planned to be randomized to each group (201 for each group). Analyses were to be performed using the Full Analysis set, Per-Protocol Analysis set and Safety Analysis set defined as follows:

- Full Analysis set: Subjects who received at least 1 dose of study drug in this study and underwent the efficacy assessment (MSQ assessment) once or more after the second visit (Wk 0), without any deviation of key inclusion/exclusion criteria
- Per-Protocol Analysis set: Compliant subjects who may be characterized by the absence of any major protocol violations including violation of inclusion/exclusion criteria and the availability for primary efficacy assessment with the MSQ score adjusted according to the criteria for missing data handling
- Safety Analysis set: All subjects who received at least 1 dose of study drug

STUDY POPULATION:

This clinical study was performed at 15 hospitals across the nation between 10 Jul, 2012 and 24 Jun, 2013. Of 18 subjects screened, 13 (72.22%) were randomized to the switching group or the control group. A total of 10 subjects (55.56%) completed the study, and 3 were withdrawn for symptom aggravation (1, 5.56%) and adverse events (2, 11.11%) [Figure 1].

Figure 1. Study Flow Chart and Patient Disposition



* The reason of screening failure: Withdrawal of consent (3), deviation of inclusion/exclusion criteria (1), others: lost to follow up (1)

Demographic information of the 13 subjects included in the Safety Analysis set is presented in Table 2. The participants of this study consisted of 6 (46.2%) males and 7 (53.9%) females, and mean age (±SD) was 39.2±7.6 years (range, 25-51).

Table 2. Demographics (Safety Analysis set)

	Switching group (N=8)	Control group (N=5)	Total (N=13)
Sex , N(%)	8	5	13
Male	5 (62.5)	1 (20.0)	6 (46.2)
Female	3 (37.5)	4 (80.0)	7 (53.9)
Age (year)			
Number	8	5	13
Mean(SD)	42.3 (6.7)	34.2 (6.7)	39.2 (7.6)
median	41	34	37
Min~Max	35 ~51	25 ~42	25 ~51
Height (cm)			
Number	8	5	13

	Switching group (N=8)	Control group (N=5)	Total (N=13)
Mean(SD)	167.0 (7.1)	162.4 (4.5)	165.2 (6.5)
median	167.3	160.0	165.0
Min~Max	155.0 ~176.2	158.0 ~169.0	155.0 ~176.2
Weight (kg)			
Number	8	4	12
Mean(SD)	74.5 (13.6)	71.8 (4.6)	73.6 (11.2)
median	74.2	71.7	73.6
Min~Max	57.5 ~96.2	67.0 ~76.9	57.5 ~96.2

EFFICACY RESULTS:

Primary result

Although the efficacy assessment was supposed to be performed using the Full Analysis set and Per-Protocol Analysis set, statistical test was not available due to lack of enrollment than planned. The MSQ scores of 13 subjects at each visit are present in Table 3.

Table 3. MSQ score by subject and visit

SCR NO	Group	Visit 2 (Day 1)	Visit 3 (Day 15±3)	Visit 4 (Day 29 ±7)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
04-S-02	Switching group	3	5	2	2	5	.
04-S-03	Switching group	3	4	5	6	5	.
04-S-07	Switching group	3	5	5	6	6	.
04-S-08	Switching group	3	2	4	.	.	.
09-S-01	Switching group	3	6	6	6	6	.
12-S-02	Switching group	5	6	6	6	5	.
13-S-02	Switching group	3	3	2	.	.	3
15-S-02	Switching group	2	.	.	.	.	2
04-S-04	Control group	2	2	2	5	3	.
04-S-05	Control group	3	3	5	5	5	.
13-S-01	Control group	2	3	3	3	5	.
13-S-04	Control group	4	4	5	5	5	.
15-S-01	Control group	3	3		5	5	.

Important secondary results

The scores of the PANSS, KDAI-10, PSP and Sleep VAS are presented in Table 4, Table 5, Table 6, Table 7 and Table 8. No statistical test was performed.

Table 4. PANSS score by subject and visit

SCR NO	Group	Visit 2 (Day 1)	Visit 4 (Day 29 ±7)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
04-S-02	Switching group	58	55	79	68	.
04-S-03	Switching group	118	107	104	115	.
04-S-07	Switching group	69	66	53	53	.
04-S-08	Switching group	81	83	.	.	.
09-S-01	Switching group	60	44	36	33	.

SCR NO	Group	Visit 2 (Day 1)	Visit 4 (Day 29 ±7)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
12-S-02	Switching group	84	77	66	97	.
13-S-02	Switching group	87	72	.	.	88
15-S-02	Switching group	38	.	.	.	41
04-S-04	Control group	71	67	73	61	.
04-S-05	Control group	64	69	71	69	.
13-S-01	Control group	75	62	72	57	.
13-S-04	Control group	56	55	57	52	.
15-S-01	Control group	35	36	38	38	.

Table 5. KDAI-10 score by subject and visit

SCR NO	Group	Visit 2 (Day 1)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
04-S-02	Switching group	0	-8	2	.
04-S-03	Switching group	-2	2	4	.
04-S-07	Switching group	2	2	2	.
04-S-08	Switching group	-2	.	.	.
09-S-01	Switching group	2	0	2	.
12-S-02	Switching group	6	2	4	.
13-S-02	Switching group	-2	.	.	.
15-S-02	Switching group	-4	.	.	.
04-S-04	Control group	2	0	2	.
04-S-05	Control group	6	2	4	.
13-S-01	Control group	4	4	2	.
13-S-04	Control group	2	0	2	.
15-S-01	Control group	2	-2	-10	.

Table 6. PSP score by subject and visit

SCR NO	Group	Visit 2 (Day 1)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
04-S-02	Switching group	60	51	65	.
04-S-03	Switching group	21	35	35	.
04-S-07	Switching group	65	75	75	.
04-S-08	Switching group	35	.	.	.
09-S-01	Switching group	65	71	75	.
12-S-02	Switching group	65	65	65	.
13-S-02	Switching group	55	.	.	.
15-S-02	Switching group	95	.	.	.
04-S-04	Control group	35	45	55	.
04-S-05	Control group	90	90	91	.
13-S-01	Control group	71	71	61	.
13-S-04	Control group	65	65	65	.
15-S-01	Control group	65	65	75	.

Table 7. Sleep VAS: Quality of sleep score by subject and visit

SCR NO	group	Visit 2 (Day 1)	Visit 3 (Day 15±3)	Visit 4 (Day 29 ±7)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
04-S-02	Switching group	46	40	34	39	54	.
04-S-03	Switching group	83	86	72	86	79	.
04-S-07	Switching group	94	82	88	70	66	.
04-S-08	Switching group	34	22	70	.	.	.
09-S-01	Switching group	60	100	80	84	78	.
12-S-02	Switching group	81	92	89	93	88	.
13-S-02	Switching group	78	54	48	.	.	52
15-S-02	Switching group	62	.	.	.	.	56
04-S-04	Control group	49	21	8	50	88	.
04-S-05	Control group	20	22	58	21	80	.
13-S-01	Control group	49	66	70	86	53	.
13-S-04	Control group	93	89	91	81	70	.
15-S-01	Control group	83	76	45	52	50	.

Table 8. Sleep VAS: Daytime drowsiness score by subject and visit

SCR NO	group	Visit 2 (Day 1)	Visit 3 (Day 15±3)	Visit 4 (Day 29 ±7)	Visit 5 (Day 57 ±7)	Visit 6 (Day 85 ±7)	Withdrawal visit
04-S-02	Switching group	21	10	17	35	50	.
04-S-03	Switching group	28	15	44	42	30	.
04-S-07	Switching group	50	9	7	60	70	.
04-S-08	Switching group	53	58	28	.	.	.
09-S-01	Switching group	10	0	7	28	48	.
12-S-02	Switching group	52	12	11	9	22	.
13-S-02	Switching group	44	48	48	.	.	57
15-S-02	Switching group	56	.	.	.	.	57
04-S-04	Control group	18	36	10	14	59	.
04-S-05	Control group	80	82	74	87	70	.
13-S-01	Control group	70	29	98	79	52	.
13-S-04	Control group	6	25	23	17	50	.
15-S-01	Control group	50	36	69	62	54	.

SAFETY RESULTS:

A total of 13 subjects who received at least 1 dose of study drug were included in the adverse event (AE) and other safety assessments. Sixteen AEs were reported in 8 subjects (61.5%) and 7 adverse drug reactions (ADRs) in 5 subjects (38.5%). No serious AE (SAE) or death was reported during the study period [Table 9].

Table 9. Summary of adverse events (Safety Analysis set)

	Switching group (N=8)			Control group (N=5)			Total (N=13)		
	Incidence	(%)	Frequency	Incidence	(%)	Frequency	Incidence	(%)	Frequency

	Switching group (N=8)			Control group (N=5)			Total (N=13)		
	Incidence	(%)	Frequency	Incidence	(%)	Frequency	Incidence	(%)	Frequency
AE	5	(62.5)	11	3	(60.0)	5	8	(61.5)	16
ADR	4	(50.0)	6	1	(20.0)	1	5	(38.5)	7
	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0
Death from SAE	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0
Treatment discontinuation due to AEs	1	(12.5)	1	0	(0.0)	0	1	(7.7)	1

Overall incidence of AEs and ADRs reported during the study period is summarized in Table 10. The incidence of AEs by severity, outcome, action taken and causal relationship is presented in Table 11, Table 12, Table 13 and Table 14.

Table 10. Incidence of AEs and ADRs by organ system (Safety Analysis set)

	Switching group						Control group					
	AE			ADR			AE			ADR		
	Incidence	(%)	Frequency	Incidence	(%)	Frequency	Incidence	(%)	Frequency	Incidence	(%)	Frequency
Total	**5**	**(62.5)**	**11**	**4**	**(50.0)**	**6**	**3**	**(60.0)**	**5**	**1**	**(20.0)**	**1**
Psychiatric disorders	**4**	**(50.0)**	**7**	**2**	**(25.0)**	**2**	**1**	**(20.0)**	**1**	**0**	**(0.0)**	**0**
Insomnia	2	(25.0)	2	1	(12.5)	1	1	(20.0)	1	0	(0.0)	0
Hallucination, auditory	2	(25.0)	2	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0
Anxiety	1	(12.5)	1	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0
Impulsive behavior	1	(12.5)	1	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0
Schizophrenia*	1	(12.5)	1	1	(12.5)	1	0	(0.0)	0	0	(0.0)	0
Nervous system disorders	**2**	**(25.0)**	**3**	**2**	**(25.0)**	**3**	**1**	**(20.0)**	**1**	**0**	**(0.0)**	**0**
Somnolence	1	(12.5)	1	1	(12.5)	1	1	(20.0)	1	0	(0.0)	0
Akathisia	1	(12.5)	1	1	(12.5)	1	0	(0.0)	0	0	(0.0)	0
Extrapyramidal disorder	1	(12.5)	1	1	(12.5)	1	0	(0.0)	0	0	(0.0)	0
Investigations	**0**	**(0.0)**	**0**	**0**	**(0.0)**	**0**	**2**	**(40.0)**	**2**	**1**	**(20.0)**	**1**
Weight increased	0	(0.0)	0	0	(0.0)	0	2	(40.0)	2	1	(20.0)	1
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**0**	**(0.0)**	**0**	**1**	**(20.0)**	**1**	**0**	**(0.0)**	**0**
Hypertriglyceridaemia	1	(12.5)	1	1	(12.5)	1	0	(0.0)	0	0	(0.0)	0
Increased appetite	1	(12.5)	1	1	(12.5)	1	1	(20.0)	1	0	(0.0)	0

* Schizophrenia symptom aggravation

Table 11. Incidence of AEs by severity (Safety Analysis set)

	Switching group								Control group							
	Mild		Moderate		Severe		Total		Mild		Moderate		Severe		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Total	**0**	**(0.0)**	**10**	**(90.9)**	**1**	**(9.1)**	**11**	**(100.0)**	**4**	**(80.0)**	**1**	**(20.0)**	**0**	**(0.0)**	**5**	**(100.0)**
Psychiatric disorders	0	(0.0)	6	(54.5)	1	(9.1)	7	(63.6)	0	(0.0)	1	(20.0)	0	(0.0)	1	(20.0)
Insomnia	0	(0.0)	2	(18.2)	0	(0.0)	2	(18.2)	0	(0.0)	1	(20.0)	0	(0.0)	1	(20.0)
Hallucination, auditory	0	(0.0)	1	(9.1)	1	(9.1)	2	(18.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Anxiety	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Impulsive behavior	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Schizophrenia	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	0	(0.0)	3	(27.3)	0	(0.0)	3	(27.3)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Somnolence	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Akathisia	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Extrapyramidal disorder	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(40.0)	0	(0.0)	0	(0.0)	2	(40.0)
Weight increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(40.0)	0	(0.0)	0	(0.0)	2	(40.0)
Metabolism and nutrition disorders	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hypertriglyceridaemia	0	(0.0)	1	(9.1)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Increased appetite	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)

Table 12. Incidence of AEs by outcome (Safety Analysis set)

	Switching group													Control group										
	Recovered/ resolved		Recovered/ resolved with sequelae		Recovering/resolving		Not recovered/ not resolved		Fatal		Unknown		Total	Recovered/ resolved		Recovered/resolved with sequelae		Recovering/resolving		Not recovered/ not resolved		Fatal		Unknown		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N (%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Total	**7**	**(63.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**4**	**(36.4)**	**0**	**(0.0)**	**0**	**(0.0)**	**11 (100.0)**	**3**	**(60.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(40.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(100.0)**
Psychiatric disorders	4	(36.4)	0	(0.0)	0	(0.0)	3	(27.3)	0	(0.0)	0	(0.0)	7 (63.6)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Insomnia	2	(18.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2 (18.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hallucination, auditory	0	(0.0)	0	(0.0)	0	(0.0)	2	(18.2)	0	(0.0)	0	(0.0)	2 (18.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Anxiety	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1 (9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Impulsive behavior	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1 (9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Schizophrenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1 (9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	3	(27.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	3 (27.3)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Somnolence	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1 (9.1)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Akathisia	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1 (9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Extrapyramidal disorder	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1 (9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0 (0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	2	(40.0)
Weight increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0 (0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	2	(40.0)
Metabolism and nutrition disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1 (9.1)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hypertriglyceridaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1 (9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Increased appetite	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0 (0.0)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)

Table 13. Incidence of AEs by action taken (Safety Analysis set)

	Switching group																							
	Drug withdrawn		Drug interrupted		Dose reduced		Dose increased		Dose not changed		Unknown		Not applicable		Total		Drug withdrawn		Drug interrupted		Dose reduced		Dose increased		Dose not changed		Unknown		Not applicable		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Total	**1**	**(9.1)**	**3**	**(27.3)**	**1**	**(9.1)**	**3**	**(27.3)**	**3**	**(27.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**11**	**(100.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(100.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(100.0)**
Psychiatric disorders	1	(9.1)	1	(9.1)	0	(0.0)	3	(27.3)	2	(18.2)	0	(0.0)	0	(0.0)	7	(63.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Insomnia	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	2	(18.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hallucination, auditory	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	2	(18.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Anxiety	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Impulsive behavior	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Schizophrenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	0	(0.0)	2	(18.2)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(27.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Somnolence	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Akathisia	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Extrapyramidal disorder	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(40.0)	0	(0.0)	0	(0.0)	2	(40.0)
Weight increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(40.0)	0	(0.0)	0	(0.0)	2	(40.0)
Metabolism and nutrition disorders	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hypertriglyceridaemia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Increased appetite	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	1	(20.0)

Table 14. Incidence of AEs by causal relationship (Safety Analysis set)

	Switching group												Control group											
	Not related		Doubtful		Possible		Probable		Very likely		Total		Not related		Doubtful		Possible		Probable		Very likely		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Total	**0**	**(0.0)**	**5**	**(45.5)**	**6**	**(54.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**11**	**(100.0)**	**1**	**(20.0)**	**3**	**(60.0)**	**1**	**(20.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(100.0)**
Psychiatric disorders	0	(0.0)	5	(45.5)	2	(18.2)	0	(0.0)	0	(0.0)	7	(63.6)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Insomnia	0	(0.0)	1	(9.1)	1	(9.1)	0	(0.0)	0	(0.0)	2	(18.2)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hallucination, auditory	0	(0.0)	2	(18.2)	0	(0.0)	0	(0.0)	0	(0.0)	2	(18.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Anxiety	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Impulsive behavior	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Schizophrenia	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	0	(0.0)	0	(0.0)	3	(27.3)	0	(0.0)	0	(0.0)	3	(27.3)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Somnolence	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Akathisia	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Extrapyramidal disorder	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	1	(20.0)	0	(0.0)	0	(0.0)	2	(40.0)
Weight increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	1	(20.0)	0	(0.0)	0	(0.0)	2	(40.0)
Metabolism and nutrition disorders	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)
Hypertriglyceridaemia	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	1	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Increased appetite	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)

Study Limitation:

Although a total of 402 subjects were required to test the hypothesis of this study, only 13 subjects were randomized to either treatment or control group; therefore, we could not test the hypothesis.

CONCLUSION:

This clinical study was conducted to compare the changes in patient satisfaction between immediate or delayed switching to paliperidone ER in schizophrenia patients dissatisfied with previous antipsychotic drugs, but terminated early due to insufficient enrollment required for hypothesis testing.

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STUDY TITLE:	An open-label, prospective, randomized and comparative study of patient satisfaction between continued administration of previous antipsychotics versus switched administration to paliperidone ER in non-satisfied schizophrenia patients with previous antipsychotic drug
REPORT CONTRIBUTORS:	Lee, SunKyoung, CRA(Medical Writer); Kim, SuYoun, MS(Statistician)

SPONSOR'S RESPONSIBLE MEDICAL OFFICER

NAME:	Lee, EunJung. MD. PhD
TITLE:	TAP

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

SIGNATURE:

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