Johnson & Johnson Taiwan Ltd.

Synoptic Clinical Study Report

A Randomized, Open-Label, Study to Evaluate the Effect of Oral Paliperidone Extended-Release and Oral Risperidone Immediate-Release on Selected Cognitive Domains in Clinically Stable Subjects with Schizophrenia

Protocol R076477SCH4066; Phase 4

R076477 (paliperidone ER)

COORDINATING INVESTIGATOR: [redacted], MD, MS - [redacted] Taiwan

SPONSOR'S RESPONSIBLE MEDICAL OFFICER: [redacted], MD

DATE STUDY INITIATED: 28 December 2012

DATE STUDY COMPLETED: 02 June 2015

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GCP Compliance: This study was conducted in compliance with Good Clinical Practice, including the archival of essential documents.

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Protocol No.: R076477SCH4066

Title of Study: A Randomized, Open-Label, Study to Evaluate the Effect of Oral Paliperidone Extended-Release and Oral Risperidone Immediate-Release on Selected Cognitive Domains in Clinically Stable Subjects with Schizophrenia

Name of Active Ingredient(s): R076477 (paliperidone ER)

NCT No.: NCT01670071

Clinical Registry No.: CR100817

Coordinating Investigator: [redacted], MD, MS - [redacted]

Study Center(s): The study was conducted at 3 sites in Taiwan. A list of sites is provided in Appendix 4.

Publication (Reference): None

Study Period: 28 December 2012 to 02 June 2015. Database lock date: 07 September 2015

Phase of Development: 4

OBJECTIVES:

The objectives of this study were to compare the effect of oral paliperidone extended-release (ER) and oral risperidone immediate-release (IR) on cognitive function in subjects with an established diagnosis of schizophrenia.

The primary objective of this study was to compare the change from baseline in category fluency of the Cognitive Abilities Screening Instrument, Chinese version (CASI C-2.0) between paliperidone ER and risperidone IR after 24-weeks treatment in schizophrenia subjects.

The secondary objectives of this study were to explore additional cognitive, efficacy endpoints (the abstraction and judgment and other domains of CASI C-2.0, Modified Wisconsin Card Sorting Test [MWCST], Continuous Performance Test [CPT], Positive and Negative Syndrome Scale [PANSS], Clinical Global Impression-Severity [CGI-S], Personal and Social Performance scale [PSP], and Medication Satisfaction Questionnaire [MSQ]) and tolerability outcomes in schizophrenia subjects treated with paliperidone ER or risperidone IR up to 24 weeks.

HYPOTHESIS:

Paliperidone ER was hypothesized to be superior to risperidone IR in improving category fluency of the CASI C-2.0 at the end of the study (Week 24).

METHODS:

This clinical study was a 28-week, randomized, open-label, active-controlled comparative study. The study was conducted at 3 sites in Taiwan. The study was expected to enroll approximately 50 subjects diagnosed with schizophrenia based on the diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV).

All eligible subjects entered a run-in period to receive a stable therapeutic dose of oral risperidone IR for at least 4 weeks. After the 4-week run-in period, subjects who met all inclusion and none of the exclusion criteria at baseline (Week 0, randomization day) were randomly assigned in a 1:1 ratio to either remain on oral risperidone IR or to a therapeutic dose of paliperidone ER and prospectively followed for a 24-week

treatment phase. The treatment phase was composed of a 4-week flexible dose period followed by a 20-week stable dose period. During the first 4 weeks of the treatment phase, the investigator was allowed to increase or decrease the dose of paliperidone ER or risperidone IR for each subject. At the end of 4-week flexible dose period, the final dose was to be maintained for the 20-week fixed-dose period. However, dose adjustment was allowed if clinically indicated (eg, significant side effects emerged or there was evidence of a lack of efficacy). Efficacy and safety were assessed during 4 visits at baseline (Week 0) and Weeks 4, 12, and 24. Details on the timing of the treatment and assessments are given in the Time and Events Schedule located in the protocol (Appendix 1).

A major protocol deviation that impacted the achievement of study objectives was identified during the study. The PANSS, CGI-S, and PSP were not evaluated by blinded-raters according to protocol design. The departure from the protocol design was considered serious enough to impact efficacy result interpretation. Therefore, the efficacy analysis was not performed.

Other significant deviations included randomization of 5 subjects who did not meet inclusion/exclusion criteria.

Number of Subjects (Planned and Analyzed):

Planned: Fifty subjects were planned to be enrolled in the study.

Analyzed: A total of 17 subjects were randomized and included in the safety and intent-to-treat (ITT) population.

Diagnosis and Main Criteria for Inclusion:

Subjects (male or female ≥20 and ≤60 years of age) with established diagnosis of schizophrenia (diagnosis criteria: DSM-IV), CASI C-2.0 total score between 50 and 85 (inclusive) at baseline, PANSS total score between 60 and 85 (inclusive), and CGI-S change ≤1 in the month prior to randomization were eligible for enrolment in this study. In addition, they were required to be on a stable therapeutic dose of oral risperidone IR (between 3-6 mg/day) for at least 4 weeks prior to randomization. Only subjects who were non-acute but symptomatic were allowed to take part in the study. Refer to the study protocol (Appendix 1) for a complete list of inclusion and exclusion criteria.

Test Product, Dose and Mode of Administration, Batch No.:

Paliperidone ER was administered orally with or without food. Once it was decided to take with or without food, it was recommended to maintain this pattern consistently.

After randomization, if subjects were switched from risperidone IR to paliperidone ER, the corresponding dose level for paliperidone ER was assigned as the starting dose in the 4-week flexible dose period (see Table 1). During the 20-week fixed-dose period, the subjects' dose level adjustment was allowed, if necessary. Lot numbers (with expiration dates) for paliperidone ER 3 mg were DDZSS00 (31 March 2015) and ECZSG00 (29 February 2016), paliperidone ER 6 mg were DCZSU00 (28 February 2015) and DKZSB00 (31 October 2015), and paliperidone ER 9 mg were DGZS500 (31 May 2015) and EDZSD01 (31 March 2016).

Table 1: Corresponding Dosages of Paliperidone ER and Risperidone IR

Study Drugs	Dosing time	Approximate Corresponding Dosages			
Risperidone IR	AM	1 mg	2 mg	2 mg	3 mg
	PM	2 mg	2 mg	3 mg	3 mg or 4 mg
	Daily total	**3 mg**	**4 mg**	**5 mg**	**6 mg or 7 mg**
Paliperidone ER	q.d.	**6~9 mg**	**9~12 mg**	**12 mg**	**12 mg**

IR = immediate-release; ER = extended-release; q.d.= once daily

Reference Therapy, Dose and Mode of Administration, Batch No.:

Risperidone IR was administered orally with or without food. Once it was decided to take with or without food, it was recommended to maintain this pattern consistently.

If the subject was on another antipsychotic agent (except for risperidone IR) before the run-in period, the agent was discontinued within 2 weeks after subject entered the run-in period. All eligible subjects entered the run-in period and received a stable therapeutic dose of oral risperidone IR (between 3-6 mg/day) for at least 4 weeks. Adjustment of the dosage was done at the investigator's discretion, based on the individual subject's clinical response and tolerability to risperidone IR. The dose level equivalence of risperidone IR and paliperidone ER is presented in Table 1. Lot numbers (with expiration dates) for risperidone IR 2 mg were 17335 (05 June 2015) and 17838 (05 March 2016) and risperidone IR 3 mg were 17268 (27 May 2015) and 18115 (07 July 2016)

Duration of Treatment:

The total study duration was 28-week (including a 4-week run-in period, and a 24-week treatment phase composed of a 4-week flexible dose period followed by a 20-week stable dose period).

Criteria for Evaluation:

Efficacy Evaluations/Endpoints

The primary efficacy endpoint was the change in category fluency score of cognitive function scale (CASI C-2.0) from baseline to Week 24.

The secondary efficacy endpoints were:

- The change in abstraction and judgment score and other domains of cognitive function scale (CASI C-2.0) from baseline to Week 24.
- The change from baseline in other cognitive performance and social functioning scales (CASI C-2.0, MWCST, CPT, and PSP[3]).
- The change from baseline in psychiatric assessment scales (PANSS,[1,2] CGI-S) and MSQ.

Safety Evaluations

Safety was evaluated by monitoring of adverse events (AEs), extrapyramidal symptoms (using Extrapyramidal Symptoms Rating Scale [ESRS]), vital sign measurements, physical and neurological examinations, and pregnancy test for women of child bearing potential women.

Data Quality Assurance:

The study was monitored according to the sponsor's current Standard Operating Procedure for the Monitoring of Clinical Trials. Steps taken to ensure the accuracy and reliability of the clinical study data included the selection of qualified investigators and appropriate study sites, review of protocol procedures with the investigator and associated study-site personnel prior to study start, and periodic monitoring visits by the sponsor or their delegate. The study-specific monitoring guidelines are stored in the trial master file (TMF).

During the course of this study, several activities were implemented to ensure proper operational study oversight (documented in the TMF). These activities were focused on identification and resolution of operational and quality issues to ensure data integrity, protocol compliance, and safety of the study participants.

Written instructions were provided for the collection of source documentation. Source documentation was reviewed for accuracy and completeness by the sponsor during on-site monitoring visits and internal data

reviews by various functions throughout the study and at the time of database lock. Discrepancies were resolved with the investigator or designees, as appropriate.

Statistical Methods:

Analysis Sets: All randomized subjects who received at least 1 dose of study agent during the treatment phase (paliperidone ER or risperidone IR) and had at least 1 efficacy evaluation after baseline were to be included in the ITT population. Efficacy analyses were to be performed on the ITT population.

All subjects who were treated with paliperidone ER or risperidone IR at least once during the run-in period or treatment phase were to be included in the safety population. The safety analyses were performed on the safety population according the actual study agent received.

Sample Size Determination: Since this was a pilot study, no formal power calculation had been applied. According to a previous cognitive study in Taiwan, 13 of 13 (100%) subjects had demonstrated clinically meaningful improvement in category fluency in CASI change from baseline (about 1.77 scores) after subjects received paliperidone ER for 24 weeks followed by oral risperidone IR alone for 4 weeks.[4] Therefore, 25 enrolled subjects per group were considered sufficient to identify a signal in change of the cognitive performance measure. In case a high number of non-evaluable subjects did not meet the ITT criteria described above, additional subjects could be enrolled.

Demographic and Other Baseline Characteristics: The demographic and baseline characteristics including age, gender, height, weight, and education level collected at screening visit were summarized for ITT population by treatment group. Summary statistics (N, mean, median, standard deviation (SD), and range) were generated for continuous variables (eg, age and weight). The number and percentage of subjects were presented for categorical variables (eg, gender and education level).

Efficacy: The primary efficacy variable was to evaluate the change in category fluency score of cognitive function scale (CASI C-2.0) from baseline to Week 24.

The secondary efficacy endpoint was the change in abstraction and judgment score and other domains of cognitive function scale (CASI C-2.0) from baseline to Week 24.

The other secondary efficacy endpoint was the change from baseline in other cognitive performance and social functioning scales (CASI C-2.0, MWCST, CPT, and PSP), psychiatric assessment scales (PANSS, CGI-S) and MSQ. During the 24-weeks treatment phase, CASI C-2.0 was assessed at baseline, Week 4, 12, 24; the other efficacy variables were evaluated at designated visits.

Since the PANSS, CGI-S, and PSP were not evaluated by blinded-raters according to protocol design and study was terminated prematurely by the sponsor, all the efficacy variables were presented by listing, and statistical analysis was not performed.

Safety: AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA), Version 18.0. The number and percentage of subjects with any AEs were summarized by system organ class (SOC) and preferred term, in addition, by severity (mild, moderate, severe), and by relationship to study agent for each treatment group. The treatment-emergent adverse events (TEAEs) that occurred during run-in phase and treatment phase were summarized. Separate summaries were generated for treatment-related (possible, probable, or very likely) AEs overall and by severity. The listings of subjects with serious adverse events (SAEs) and discontinuation due to AEs that occurred during the study were presented.

The ESRS was summarized by treatment group at each designated visit. Descriptive statistics were presented for different domains of ESRS (dystonia; dyskinetic movement; clinical global impression of severity of dyskinesia, Parkinsonism, dystonia, akathisia) and the total score.

Vital signs (including heart rate, blood pressure, and body temperature) and weight were summarized by treatment group at each visit. Physical and neurological examination findings were provided by a status transition table (normal, abnormal, not done) from screening visit to baseline. No statistical analyses were performed.

RESULTS:

STUDY POPULATION:

This study was conducted from 28 December 2012 to 02 June 2015 in 3 sites in Taiwan. Fifty subjects were planned to be enrolled in the study. However, the study was terminated prematurely by the sponsor after the enrollment of 17 subjects due to slow enrollment and having no rater-blinded efficacy evaluations. Subject disposition data are summarized for all randomized subjects in Table 2. All 17 subjects (100%) completed the 4-week run-in period and were randomized in a 1:1 ratio to either remain on oral risperidone IR (10 subjects) or to a therapeutic dose of paliperidone ER (7 subjects). All subjects (17) received at least 1 dose of study agent during the run-in period and treatment phase and had at least 1 efficacy evaluation after baseline, therefore by definition represents the safety and ITT population for this study (Attachment Table 03). Of the 17 subjects (100%), 6 subjects (35.3%) completed the study and 11 subjects (64.7%) were withdrawn from the study. Nine subjects (52.9%) were withdrawn due to "Other" reasons and 2 subjects (11.8%) were withdrawn due to withdrawal of consent. The "Other" reasons for withdrawal from the study were as follows:

- Study termination (6 subjects [35.3%])
- Not met inclusion criterion number 3 of the protocol, ie, not having CASI C-2.0 total score between 50 and 85 (inclusive) at baseline (Appendix 1; 2 subjects [11.8%])
- Not met exclusion criterion number 4 of the protocol, ie, the subject had taken paliperidone ER in the past (Appendix 1; 1 subject [5.9%]).

Table 2: Summary of Subject Disposition (Randomized)

	Paliperidone N=7	Risperidone N=10	All Subjects N=17
Visit 1 (Screening)	7 (100.0%)	10 (100.0%)	17 (100.0%)
Visit 2 (Baseline)	7 (100.0%)	10 (100.0%)	17 (100.0%)
Visit 3 (Week 4)	5 (71.4%)	10 (100.0%)	15 (88.2%)
Visit 4 (Week 12)	2 (28.6%)	8 (80.0%)	10 (58.8%)
Visit 5 (Week 24)	1 (14.3%)	5 (50.0%)	6 (35.3%)
Withdrawal from Study	6 (85.7%)	5 (50.0%)	11 (64.7%)
Reason for Withdrawal from Study			
Withdrawal consent	2 (28.6%)	0 (0.0%)	2 (11.8%)
Other	4 (57.1%)	5 (50.0%)	9 (52.9%)
Study Termination	1 (14.3%)	5 (50.0%)	6 (35.3%)
Not Met Inclusion No. 3	2 (28.6%)	0 (0.0%)	2 (11.8%)
Not Met Exclusion No. 4	1 (14.3%)	0 (0.0%)	1 (5.9%)

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A listing of primary reasons for prematurely discontinued subjects is provided in Appendix 13 (Listing 01-2). Listings of study visit information and inclusion/exclusion criteria for all screened subjects are provided in Appendix 16 (Listing 01-1 and Listing 04, respectively).

Demographic and baseline characteristics are presented in Attachment Table 04. Of the 17 subjects in the ITT analysis set, 12 (70.6%) were male and 5 (29.4%) were female. The mean (SD) age was 45.9 (8.6) years, the mean (SD) weight was 68.9 (12.8) kg, and the mean body mass index was 25.5 (4.6) kg/m^2. Of the highest education level that the 17 subjects received, 9 subjects (52.9%) had attended senior high school, 6 subjects (35.3%) had attended junior high school, and 2 subjects (11.8%) had attended elementary school. At baseline, the majority of subjects had CGI-S score (10 subjects [58.8%]) and MSQ score (14 subjects [82.4%]) of 4. The mean (SD) CPT score at baseline was 769.0 (209.1) in the paliperidone ER group and 947.0 (332.9) in the risperidone IR group. There was no notable difference at baseline in the other efficacy variables (including CASI C-2.0, PANSS, PSP, and MWCST) between the 2 treatment groups.

Demographic characteristics are listed for each subject in Appendix 16 (Listing 02).

A summary of protocol deviations and description of individual protocol deviations is provided in Appendix 14 (Table 02). All 17 subjects (100%) had the protocol deviation of having no rater-blinded evaluations of PANSS, CGI-S, and PSP. Five subjects did not meet inclusion/exclusion criteria, but were randomized to the paliperidone ER group. Of these 5 randomized subjects, 1 was treated with clozapine within 3 months before randomization (met the exclusion criterion number 5 of the protocol [Appendix 1]), 1 received paliperidone ER in the past (met the exclusion criterion number 4 of the protocol), 1 subject each had been randomized with a CASI C-2.0 score of 93 and 90, respectively, (did not met the inclusion criterion number 3 of the protocol), and 1 subject did not receive a stable therapeutic dose of oral risperidone IR for at least 4 weeks prior to randomization (did not met the inclusion criterion number 6 of the protocol). One of these 5 subjects in the paliperidone ER group had medication overdose of having 16 medications more than that specified in the protocol.

Based on the review of the data by the study team, the protocol deviation of having no rater-blinded evaluations had compromised the efficacy results interpretation; so this study was terminated prematurely by sponsor. Given the low frequency of other deviations, no effect on the safety findings of this study was expected.

During the run-in phase, the mean (SD) duration of exposure in the risperidone IR group was 28 (0.0) days and the mean (SD) total dose of risperidone IR received by subjects was 102 (22.1) mg. During the treatment phase, the mean (SD) duration of exposure in the paliperidone ER group was 68 (50.6) days and in the risperidone IR group was 124 (52.8) days; and the mean total dose of study agent (paliperidone ER or risperidone IR) received by subjects was similar between the 2 treatment groups (Attachment Table 07).

Three of the 17 subjects had study agent dose adjustment/interruption during the study (Appendix 17 [Listing 15]). Of these 3 subjects, 2 subjects were in the paliperidone ER group and 1 subject was in the risperidone IR group.

A listing of drug accountability is provided in Appendix 17 (Listing 14).

Of the psychiatric history of the 17 subjects, 10 subjects (58.8%) had paranoid schizophrenia, 4 subjects (23.5%) had undifferentiated schizophrenia, 2 subjects (11.8%) had residual schizophrenia, and 1 subject (5.9%) had disorganized schizophrenia (Attachment Table 05). A listing of subject diagnosis and psychiatric history is provided in Appendix 16 (Listing 03). Medical history abnormalities are listed by subject in Appendix 16 (Listing 05). Summaries of all medical conditions and active medical conditions are provided in Attachment Table 06-1 and Attachment Table 06-2, respectively.

Listings of concomitant medications prior to study agent administration and after randomization are provided in Appendix 16 (Listing 16-1 and Listing 16-2, respectively). Listings of physical/neurological examination, physical examination abnormality, neurological examination abnormality are provided in Appendix 16 (Listing 06-1, Listing 06-2, and Listing 06-3, respectively).

EFFICACY RESULTS:

Due to the protocol deviation of not having rater-blinded evaluations and the lower number of subjects enrolled, efficacy results were not analyzed but presented in listings. Listings of CASI C-2.0, CPT, PANSS; and CGI-S, MSQ, MWCST, and PSP scores by subject are provided in Appendix 18 (Listing 07, Listing 08, Listing 09, and Listing 10, respectively).

SAFETY RESULTS:

A summary of overall AEs is presented in Table 3. Five subjects (71.4%) in the paliperidone ER group and 6 subjects (60.0%) in the risperidone IR group experienced at least 1 TEAE during the study. One subject each in the paliperidone ER and risperidone IR groups experienced at least 1 SAE. No AEs leading to death or permanent discontinuation of the study agent were reported (Appendix 19 [Table 11]). No treatment-related AEs were reported (Attachment Table 10-1 and Attachment Table 10-2). A listing of subjects who experienced AEs during the study is provided in Appendix 19 (Listing 13).

Table 3: Summary of Overall Adverse Events (Safety)

	Paliperidone N=7		Risperidone N=10		All Subjects N=17	
	Event	Subject	Event	Subject	Event	Subject
Run-in Phase						
Any AE	5	5 (71.4%)	2	2 (20.0%)	7	7 (41.2%)
Treatment-Related AE	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
Serious AE	1	1 (14.3%)	0	0 (0.0%)	1	1 (5.9%)
Discontinuation due to AE	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
AE leading to death	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
Treatment Phase						
Any AE	3	3 (42.9%)	16	6 (60.0%)	19	9 (52.9%)
Treatment-Related AE	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
Serious AE	1	1 (14.3%)	3	1 (10.0%)	4	2 (11.8%)
Discontinuation due to AE	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
AE leading to death	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
Overall Study						
Any AE	8	5 (71.4%)	18	6 (60.0%)	26	11 (64.7%)
Treatment-Related AE	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
Serious AE	2	1 (14.3%)	3	1 (10.0%)	5	2 (11.8%)
Discontinuation due to AE	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
AE leading to death	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)

Related to Study Drug: Possible, Probable, Very Likely
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During the run-in phase, 5 subjects (71.4%) in the paliperidone ER group and 2 subjects (20.0%) in the risperidone IR group experienced a TEAE (Attachment Table 09-1). One subject (14.3%) in the paliperidone ER group experienced an SAE (Table 3). The SOC with the highest incidence of TEAEs was Gastrointestinal disorders (total: 4 subjects [23.5%]; paliperidone ER group: 3 subjects [42.9%]; risperidone IR group: 1 subject [10.0%]). The most commonly (occurred in ≥2 subjects) reported TEAEs

were toothache (1 subject each in the paliperidone ER and risperidone IR groups) and nasopharyngitis (1 subject each in the paliperidone ER and risperidone IR groups).

During the treatment phase, 3 subjects (42.9%) in the paliperidone ER group and 6 subjects (60.0%) in the risperidone IR group experienced at least 1 TEAE (Attachment Table 09-2). One subject each in the paliperidone ER and risperidone IR groups experienced at least 1 SAE (Table 3). The SOCs with the highest incidence of TEAEs were Gastrointestinal disorders (total: 3 subjects [17.6%]; risperidone IR group: 3 subject [30.0%]) and Infections and infestations (total: 3 subjects [17.6%]; risperidone IR group: 3 subjects [30.0%]). The most commonly (occurred in ≥2 subjects) reported TEAEs in these SOCs were upper respiratory tract infection (2 subjects [20.0%] in the risperidone IR group) and toothache (2 subjects [20.0%] in the risperidone IR group).

Two of the 17 subjects had at least 1 SAE (1 subject each in the paliperidone ER and risperidone IR groups; Appendix 19 [Table 12]). In the paliperidone ER group, 1 subject had SAEs of acute abdominal pain and persecutory delusion. In the risperidone IR group, 1 subject had SAEs of cellulitis, hypopotassemia, and hyponatremia. Narratives for subjects with SAEs are provided in Attachment Subject Narratives.

Summaries of Parkinsonism and akathisia score, dystonia score, and dyskinesia score of ESRS over time are provided in Attachment Table 13-1, Attachment Table 13-2, and Attachment Table 13-3, respectively. No clinically notable change in the Parkinsonism and akathisia, dystonia, or dyskinesia scores of ESRS from baseline to end of study was observed in any of the 2 treatment groups. Listings of ESRS, Part I-II and Part III-VIII are provided in Appendix 20 (Listing 11-1 and Listing 11-2, respectively).

Summaries of CGI-S of Parkinsonism, akathisia, dystonia, and dyskinesia of ESRS over time are provided in Attachment Table 13-4, Attachment Table 13-5, Attachment Table 13-6, and Attachment Table 13-7, respectively. No clinically notable change in the CGI-S of Parkinsonism, akathisia, dystonia, and dyskinesia of ESRS from baseline to end of study was observed in any of the 2 treatment groups.

A summary of total score of ESRS over time is provided in Attachment Table 13-8. No clinically meaningful change in the total score of ESRS from baseline to end of study was observed in any of the 2 treatment groups.

Descriptive summaries of heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), body temperature, and body weight are provided in Attachment Table 14, Attachment Table 15, Attachment Table 16, Attachment Table 17, and Attachment Table 18, respectively. No clinically notable changes from baseline to the end of study were recorded in the mean SBP, DBP, heart rate, temperature, or weight during the study. A listing of vital signs measurements during the study is provided in the Appendix 20 (Listing 12).

Summaries of physical examination and neurological examination during run-in period are provided in Attachment Table 19 and Attachment Table 20, respectively. The majority of subjects had normal physical and neurological examinations at screening and baseline. No shifts from normal at screening to abnormal at baseline occurred in physical/neurological examination.

Study Limitations:

The study was terminated by the sponsor after the enrollment of 17 subjects due to slow enrollment and having no rater-blinded efficacy evaluations, therefore efficacy interpretation was not made.

CONCLUSIONS:

Since the PANSS, CGI-S, and PSP were not evaluated by blinded-rater according to protocol design and the study was terminated prematurely; therefore the effect of oral paliperidone ER and oral risperidone IR on the selected cognitive domains in clinically stable subjects with schizophrenia was not analyzed.

Oral paliperidone ER and risperidone IR were safe and well tolerated. No new safety signals emerged during the study.

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SIGNATURE OF SPONSOR'S RESPONSIBLE MEDICAL OFFICER

STUDY TITLE:	A Randomized, Open-Label, Study to Evaluate the Effect of Oral Paliperidone Extended-Release and Oral Risperidone Immediate-Release on Selected Cognitive Domains in Clinically Stable Subjects with Schizophrenia
REPORT CONTRIBUTORS:	Project Physician: [redacted] MD Statistician: [redacted] MS ([redacted]) Medical Writer: [redacted] PhD [redacted] MSc ([redacted])

SPONSOR'S RESPONSIBLE MEDICAL OFFICER

NAME: [redacted] MD

TITLE: [redacted]

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: [redacted]

DATE: Dec 11 2015

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