2. Synopsis

<table>
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Janssen Pharmaceutical K.K.</td><td rowspan="3">Individual Study Table Referring to Part of the Dossier
Volume:
Page:</td><td rowspan="3">(For National Authority Use Only)</td></tr>
<tr><td>Name of Finished Product:
To be determined.</td></tr>
<tr><td>Name of Active Ingredient:
Paliperidone</td></tr>
<tr><td colspan="3">Title of Study:
Clinical pharmacology study of JNS010 (Paliperidone palmitate) in patients with schizophrenia</td></tr>
<tr><td colspan="3">Investigators:
A total of 15 investigators including Masanori Ishikawa (see Appendix 16.1.4).</td></tr>
<tr><td colspan="3">Study sites:
A total of 15 study sites including National Center Hospital (Department of Psychiatry) (see Appendix 16.1.4)</td></tr>
<tr><td colspan="3">Publications: None</td></tr>
<tr><td colspan="2">Study Period:
April 28, 2009
(Date of informed consent obtained from the first subject)
March 2, 2010
(Date of final observation in the last subject)</td><td>Phase of Development:
Phase I/II
Study Type:
Clinical Pharmacology Study</td></tr>
<tr><td colspan="3">Objectives:
To investigate the pharmacokinetic and safety of paliperidone palmitate (150 mg.eq. [deltoid], 75 mg. eq. [deltoid] and 75 mg. eq. [gluteal]) after the repeated administration (4 injections) in the deltoid or gluteal muscle in patients with schizophrenia.</td></tr>
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Methodology:

This was a multicenter, open-label, randomized, parallel-group (among 3 groups, target sample size of 20 subjects per group) comparative study in patients with schizophrenia to assess the pharmacokinetic (PK) and safety profile of paliperidone palmitate.

At enrollment, the subjects were randomly assigned to Treatment A, B, or C to receive repeated administration of paliperidone palmitate (1 injection each on Days 1, 8, 36 and 64) at the Registration Center. In Treatment A, 150 mg e.q. was administered in the deltoid muscle (150 mg eq./deltoid group); in Treatment B, 75 mg e.q. was administered in the deltoid muscle (75 mg eq./deltoid group); in Treatment C, 75 mg e.q. was administered in the gluteal muscle (75 mg eq./gluteal group). In all the treatment groups, the subjects received 4 injections (1 injection each on Days 1, 8, 36 and 64) alternating between side (left /right).

Number of Subjects (planned and analyzed):

Planned: Target number of subjects accumulated: 66

Number of subjects analyzed: 60 (20 per treatment group)

Analyzed:

Number of subjects enrolled: 80

Number of subjects who received the study treatment : 76

(150 mg eq./deltoid group [n= 24]; 75 mg eq./deltoid group [n=27]; 75 mg eq./gluteal group; [n=25])

PK analysis set : 76 (Statistical analysis set for pharmacokinetics: 72)

Safety Population (SP): 76

Full analysis set (FAS): 76

Per protocol set (PPS): 76

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Diagnosis and Inclusion Criteria:

Subjects had to satisfy the following criteria to be enrolled in this study.

1. Subjects had to have the capability to provide informed consent in writing to participate in the study (consent of the patient's family member was also to be obtained if the investigator/subinvestigator considered it necessary).
2. Patients with a diagnosis of schizophrenia in accordance with the diagnostic criteria for DSM-IV-TR (295.30, 295.10, 295.20, 295.90, 295.60)
3. Patients aged 20 to 65 years (inclusive) at the time of IC (regardless of in-/out-patient setting or sex)
4. Patients whose psychiatric symptom is considered stable by the investigator/subinvestigator at the time of IC
5. Patients with a Positive and Negative Syndrome Scale (PANSS) score of ≤4 (moderate) in the following 9 items at screening: delusion, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, hostility, uncooperativeness, poor impulse control.
6. Patients with an experience of taking a risperidone formulation or a paliperidone formulation by 8 days before the initial day (Day 1) of the study treatment with the available (even if the patient's experience of using risperidone or paliperidone formulation cannot be confirmed at the time of IC, the patient was considered to meet this criterion if the patient took oral risperidone ≥1 mg/day for at least 4 days between the day of IC and 8 days before the initial day of study treatment, and if it is possible to confirm that there is no problem with the tolerability in the patient. Furthermore, due consideration was paid to the period in which concomitant use is disallowed).
7. Patients who can receive prescribed examinations, etc. as per the study schedule

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Study drugs, Dosage and Treatment Methods, Lot Numbers:

Study drugs, lot numbers:

- Study drug name: JNS010 (Paliperidone palmitate)
- Dosage form & content: Aqueous suspension injection containing paliperidone150 mg or 75 mg

Study drug	Volume of Suspension	Manufacturer's lot number	Prescription number	Storage Method (Expiry Date)
Paliperidone palmitate 150 mg	1.5 mL	8GB4J	F013	Store at room temperature (June 2010)
Paliperidone palmitate 75 mg	0.75 mL	8GB4H		

Dosage and administration:

- Route of administration: i.m. administration (in the deltoid or gluteal muscle)
- Dosage and Administration: 4 injections (1 injection each on Days 1, 8, 36 and 64) of paliperidone palmitate was administered at 150 mg in the deltoid muscle, 75 mg at the deltoid or gluteal muscles with injections alternating between side (left/right).

  Treatment A: 150 mg-150 mg-150 mg-150 mg eq./deltoid (150 mg eq./deltoid group)

  Treatment B: 75 mg-75 mg-75 mg-75 mg eq./deltoid (75 mg eq./deltoid group)

  Treatment C: 75 mg-75 mg-75 mg-75 mg eq./gluteal (75 mg eq./gluteal group)

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Duration of treatment:

Screening period:

From obtaining consent to the initiation of observation/examination and evaluation on Day 1 (initial day of the treatment)

Observation period (92 days):

From the initiation of observation/examination and evaluation, observation/examination and evaluation on Day 1 to the completion of observation/examination and evaluation on Day 92

Follow-up period (98 days):

From the completion of observation/examination and evaluation on Day 92 to that on Day 190

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Evaluation criteria:

Pharmacokinetics:

- Concentrations of plasma unchanged drug (Paliperidone palmitate), active metabolite (paliperidone) and its enantiomers (R078543 and R078544)
- PK parameters (C_{max}, t_{max} and AUC_{τ})

Evaluation items for safety:

- Adverse events (symptoms, signs)
- Laboratory tests
- Body weight, blood pressure, pulse rate, temperature
- Electrocardiogram (12-lead ECG at rest)
- Injection site reaction
- Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS)
- Visual Analog Scale (VAS)

Evaluation items for efficacy:

- PANSS
- Clinical Global Impression-Severity (CGI-S)

Statistical Methods:

1. Analysis sets

   For pharmacokinetics, the PK analysis set and statistical analysis set for pharmacokinetics were set.

   For safety, the SP was set. As analysis sets for efficacy, FAS and PPS were set, and the PPS was defined as a primary analysis set.

2. PK analyses

For plasma concentrations of the unchanged drug paliperidone palmitate (hereinafter referred to as paliperidone palmitate), active metabolite (paliperidone) and its enantiomers

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(R078543 and R078544), the following analyses were performed.

- For plasma concentrations of paliperidone palmitate, paliperidone, R078543 and R078544 and the ratio of R078543/R078544, descriptive statistics [e.g., mean, standard deviation (SD), median, minimum and maximum] at each blood sampling time were calculated by treatment group. Based on measurement values in each subject and descriptive statistics (mean and median), concentrations-time profiles of paliperidone, R078543 and R078544 were diagrammatically shown.

- Pharmacokinetic parameters were calculated from plasma concentrations of paliperidone, R078543 and R078544 in the second and fourth dose in each subject, and descriptive statistics were calculated by treatment group. For C_{max} and AUC_{τ}, the ratio of R078543/R078544 was calculated, and descriptive statistics were calculated by treatment group. Since plasma paliperidone palmitate concentrations were below quantification limit at most blood sampling points in any group, no pharmacokinetic parameters were calculated.
- For C_{max} and AUC_{τ} of plasma paliperidone, comparisons were conducted between injection sites, numbers of administration and treatment groups (dose proportionality), respectively.

3. Safety analyses

- Adverse events:

  Adverse events that newly occurred after study treatment and those that worsened after the study treatment (treatment-emergent signs and symptoms; TESS) were to be analyzed. In tabulation of adverse events, the verbatims recorded on the CRF were to be coded to the adequate terms of system organ class (SOC), preferred terms (PT), or

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lowest level terms (LLT) by Japanese version of the Medical Dictionary for Regulatory Activities published by ICH (MedDRA/J). The terms to be used should be selected from those grouped based on the MedDRA PT. The number of subjects with events, percentage of those with events, and number of adverse events were tabulated. The tabulation by severity was also conducted. The adverse events whose relationship with the study drug cannot be ruled out ("Doubtful", "Possible", "Probable", "Very likely") by the attending psychiatrist was handled as adverse drug reactions, and tabulated and analyzed in the same manner as adverse events.

- Serious adverse events, adverse events of interest (e.g., EPS-related adverse events), and adverse events leading to treatment discontinuation were tabulated.

- Laboratory tests:
  For quantitative laboratory examination items (hematology, biochemistry, and endocrinology), descriptive statistics of test value and its change from baseline (Day 1) at each examination time were calculated.
  For qualitative examination items (urinalysis), the frequency tabulation was conducted by measurement time, and a shift table between before and after treatment was generated. For the parameters with a reference range, values were grouped into low values, values within reference range, and high values, and a shift table between before and after treatment was generated by testing time.

- Body weight, blood pressure, pulse rate, temperature:
  The descriptive statistics were calculated for measurement value and its change from baseline (Day 1) by measurement time.

- ECG examination:

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For ECG parameters, the descriptive statistics were calculated for test value and its change from baseline (Day 1) by testing time. For the presence of abnormal findings in ECG, the frequency tabulation and the cross tabulation between before and after treatment were conducted by assessment time.

· Injection site reaction

The tabulation of the presence of injection site reaction (redness, swelling, induration, pain) between 30 minutes and 60 minutes from the study treatment was conducted by assessment time.

· DIEPSS

The frequency tabulation of the score for each item was conducted by assessment time. For the maximum score after the study treatment, the similar analysis was conducted.

· VAS

The descriptive statistics of VAS score were calculated by measurement time.

4. Efficacy analyses

The following analyses were to be conducted in PPS, which was the primary analysis set for efficacy. For PANSS total score, an analysis in FAS was also conducted.

· For PANSS total score, descriptive statistics were calculated for the score and its change from baseline (Day 1) at each assessment time by treatment group. For the change from baseline, an ANCOVA was conducted using treatment group as a factor and baseline score as a covariate, and the least squares mean and the 95% CI of each treatment group were calculated.

· For PANSS subscale score (positive subscale, negative subscale, general

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psychopathology subscale, Marder factor positive symptoms and negative symptoms, Marder factor disorganized thoughts, Marder factor hostility/excitement, Marder factor anxiety/ depression), descriptive statistics were calculated for the score and its change from baseline (Day 1) at each assessment time by treatment group. For the change from baseline, an ANCOVA with treatment group as a factor and baseline score as a covariate was conducted, and the least squares mean and the 95% CI of each treatment group were calculated.

- For CGI-S, the frequency tabulation was conducted for each assessment time by treatment group.

Summary – Conclusion

PK results:

The plasma concentrations of paliperidone palmitate and enantiomers of paliperidone (R078543 and R078544) after 4 injections (1 injection each on Days 1, 8, 36 and 64) in the deltoid muscle at 150 mg e.q. or 75 mg e.q. and in the gluteal muscle at 150 mg e.q. were measured in patients with schizophrenia to investigate the pharmacokinetic of paliperidone and its enantiomers.

The plasma concentrations of paliperidone palmitate after 4 injections (1 injection each on Days 1, 8, 36 and 64) of paliperidone palmitate 150 mg e.q. in the deltoid muscle and 75 mg e.q. in the deltoid or gluteal muscle were BQL at most PK sampling points in any treatment group.

In the repeated administration of paliperidone palmitate 75 mg e.q. in the deltoid muscle, the plasma concentration-time profile of paliperidone, R078543 and R078544 were consistently slightly higher compared with gluteal administration. In the initial phase of administration, the plasma concentrations after administration in the deltoid muscle increased more rapidly than in the administration in the gluteal muscle. The distributions of

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individual plasma concentration in deltoid injection and gluteal injection overlapped, and overlapped more at the 4th injection compared with the 2nd injection. The plasma concentrations of paliperidone, R078543 and R078544 in repeated administration of paliperidone palmitate 75 mg e.q. and 150 mg e.q. in the deltoid muscle increased with dose.

In the repeated administration of paliperidone palmitate 75 mg e.q., the PK parameters (C_{max} and AUC_{τ}) of plasma paliperidone were compared between the injections sites (deltoid or gluteal muscle). As a result, the ratios of the geometric mean (deltoid muscle/ gluteal muscle) were 1.25 to 1.48, and showed higher values in deltoid injection than in gluteal injection. The ratios of C_{max} and AUC_{τ} between the injection sites were 1.48 and 1.42 at the 2nd injection and 1.25 and 1.26 at the 4th injection, respectively, and were slightly lower at the 4th injection compared with the 2nd injection. At the 2nd injection, t_{max} was reached more rapidly in the deltoid injection compared with the gluteal injection.

PK parameters (C_{max} and AUC_{τ}) of plasma paliperidone were compared between different number of treatments [2nd injection (Day 8) and final dose (4th injection, Day 64)]. As a result, the parameters were similar between the 2nd injection (Day 8) and final dose (4th injection, Day 64) in any group.

In the repeated administration of paliperidone palmitate in the deltoid muscle, PK parameters (the dose was normalized to 50 mg e.q.; DN C_{max} and DN AUC_{τ}) of plasma paliperidone were compared between different doses (150 mg e.q. and 75 mg e.q.). As a result, the dose proportionality was suggested at the 2nd injection (Day 8) and final dose (4th injection, Day 64), respectively.

Safety results:

In patients with schizophrenia, 4 injections of paliperidone palmitate were administered at 150 mg in the deltoid muscle and at 75 mg in the deltoid or gluteal muscle to assess the

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safety. The treatment groups were 3 groups of the 150 mg eq./deltoid group, 75 mg eq./deltoid group, and 75 mg eq./gluteal group.

The 76 subjects who received study treatment (24 in the 150 mg eq./deltoid group, 27 in the 75 mg eq./deltoid group, and 25 in the 75 mg eq./gluteal group) were included in the SP.

Overall, adverse events occurred in 89.5% (68/76, 336 events). By treatment group, 91.7% occurred (22/24 subjects, 130 events) in the 150 mg eq./deltoid group, 92.6% (25/27 subjects, 145 events) in the 75 mg eq./deltoid group, and 84.0% (21/25 subjects, 61 events) in the 75 mg eq./gluteal group. The incidence in the 75 mg eq./gluteal group was lower and the number of events was fewer than the other 2 groups. The adverse events with higher incidences (overall incidence ≥10%) were “blood prolactin increased” 48.7% (37/76 subjects 37 events), “injection site pain” 27.6% (21/76 subject, 32 events), “nasopharyngitis” 26.3% (20/76, 27 events), “psychiatric symptom” 25.0% (19/76, 25 events), “injection site induration” 23.7% (18/76, 30 events), and “injection site erythema” 11.8% (9/76, 13 events).

Most of the adverse events were mild in severity. Severe adverse events occurred in 3 subjects (3 events), and all of them were considered as serious. The details were “psychiatric symptom” in 2 subjects (2 events) and “hyponatraemia” in 1 subject (1 event), and all of them recovered or recovering after treatment. Treatment with the study drug was discontinued only in 1 subject with the “psychiatric symptom” which appeared before the end of treatment.

Overall, adverse drug reactions occurred in 78.9% (60/76, 169 events). By treatment group, it occurred in 79.2% (19/24 subjects, 74 events) in the 150 mg eq./deltoid group, 85.2% (23/27 subjects, 67 events) in the 75 mg eq./deltoid group, and 72.0% (18/25 subjects, 28 events) in the 75 mg eq./gluteal group. The incidence in the 75 mg eq./gluteal group was lower and the number of events was fewer than the other 2 groups. The adverse drug reactions with higher incidences (overall incidence ≥ 10%) were “blood prolactin

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increased" 47.4% (36/76, 36 events), "injection site induration" 23.7% (18/76, 30 events), and "injection site pain" 22.4% (17/76, 27 events).

No deaths were observed in this study.

Overall, serious adverse events occurred in 10.5% (8/76, 11 events). By treatment group, it occurred in 12.5% (3/24 subjects, 3 events) in the 150 mg eq./deltoid group, 11.1% (3/27 subjects, 5 events) in the 75 mg eq./deltoid group, and 8.0% (2/25 subjects, 3 events) in the 75 mg eq./gluteal group. The breakdown of the events were "psychiatric symptom" 7.9% (6/76, 7 events), "hyponatraemia", "anxiety", "delusion" and "hallucination" 1.3% (1/76 subject, 1 event) each. These events were evaluated as those related to worsening of the underlying disease, except for "hyponatraemia". The subject who developed the "hyponatraemia" was complicated with polydipsia, and the subject's intake of a large amount of water before the onset of the event was considered to be the cause. However, the relationship between the polydipsia and underlying disease was not evaluated, and no other worsening in psychiatric symptom to be noted was reported. Most of the serious adverse events had occurred after the completion of study treatment, and none of them was strongly suspected of having a causal relationship with the study drug. All the events were recovered or recovering after treatment.

Overall, adverse events leading to discontinuation of treatment occurred in 3.9% (3/76, 6 events). By treatment group, it occurred in 4.2% (1/24 subject, 4 events) in the 150 mg eq./deltoid group, 7.4% (2/27 subjects, 2 events) in the 75 mg eq./deltoid group, and 0% in the 75 mg eq./gluteal group. The breakdown of the events were "insomnia", "psychiatric symptom", "injection site erythema" "injection site induration", "injection site warmth" and "injection site swelling" 1.3% (1/76 subject, 1 event) each, and they were adverse events related to worsening of the underlying disease or those related to injection site reaction.

The severe adverse event leading to discontinuation of treatment was only the "psychiatric symptom" in 1 subject (1 event), which was considered as serious. The outcomes of all the

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events were recovered without any treatment or after treatment.

Overall, EPS-related adverse events occurred in 14.5% (11/76 subject, 14 events). By treatment group, it occurred in 12.5% (3/24 subjects, 5 events) in the 150 mg eq./deltoid group, 22.2% (6/27 subjects, 6 events) in the 75 mg eq./deltoid group, and 8.0% (2/25 subjects, 3 events) in the 75 mg eq./gluteal group. The incidences of the respective events were 1.3% (1/76, 1 event) each, overall, except for "extrapyramidal disorder" 3.9% (3/76, 4 events) and "akathisia" 2.6% (2/76, 3 events). All the events were mild or moderate in severity, and no serious event was observed.

Overall, prolactin-related adverse occurred in 48.7% (37/76, 38 events). By treatment group, it occurred in 58.3% (14/24 subjects, 15 events) in the 150 mg eq./deltoid group, 48.1% (13/27 subjects, 13 events) in the 75 mg eq./deltoid group, and 40.0% (10/25 subjects, 10 events) in the 75 mg eq./gluteal group. All the events were "blood prolactin increased" except for "amenorrhoea" in 1 subject (1 event) in the 150 mg eq./deltoid group. All the events were mild in severity. No other prolactin-related clinical symptoms (e.g., gynaecomastia, ejaculation disorder, galactorrhoea) were observed. Blood prolactin concentrations increased with administration of paliperidone palmitate, and the degree of the increase was larger in women than in men.

Overall, blood glucose-related adverse events occurred in 1.3% (1/76 subject, 1 event). The event was "glucose urine present" in the 75 mg eq./deltoid group, and the severity was mild.

Overall, adverse events related to injection site reaction occurred in 40.8% (31/76, 97 events). By treatment group, it occurred in 50.0% (12/24 subjects, 52 events) in the 150 mg eq./deltoid group, 48.1% (13/27 subjects, 36 events) in the 75 mg eq./deltoid group, and 24.0% (6/25 subjects, 9 events) in the 75 mg eq./gluteal group. The incidence in the 75 mg eq./gluteal group was lower and the number of events was fewer compared with the other 2 groups. The adverse events with higher incidences (overall incidence ≥5%) were "injection site pain" 27.6% (21/76 subject, 32 events), "injection site induration" 23.7% (18/76, 30

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events), "injection site erythema" 11.8% (9/76, 13 events), "injection site swelling" 9.2% (7/76, 9 events) and "injection site warmth" 5.3% (4/76, 7 events). All the events were mild or moderate in severity, and there was no serious event.

Overall, cardiovascular system-related adverse events occurred in 7.9% (6/76, 7 events). By treatment group, it occurred in 12.5% (3/24 subjects, 3 events) in the 150 mg eq./deltoid group, 7.4% (2/27 subjects, 3 events) in the 75 mg eq./deltoid group and 4.0% (1/25 subjects, 1 event) in the 75 mg eq./gluteal group. All the incidences of the events were 1.3% (1/76 subject, 1 event) each, except for "orthostatic hypotension" 2.6% (2/76, 2 events). All the events were mild in severity, and no serious event was observed.

Over all, psychiatric symptom-related adverse events occurred in 35.5% (27/76, 41 events). By treatment group, it occurred in 29.2% (7/24 subjects, 8 events) in the 150 mg eq./deltoid group, 51.9% (14/27 subjects, 25 events) in the 75 mg eq./deltoid group, and 24.0% (6/25 subjects, 8 events) in the 75 mg eq./gluteal group. The adverse events with higher incidences (overall incidence ≥5%) were "psychiatric symptom" 25.0% (19/76, 25 events) and "insomnia" 9.2% (7/76, 8 events). The severe "psychiatric symptom" was observed in 2 subjects (2 events), and the both events were considered as serious adverse events.

In laboratory test values in the hematology, biochemistry, urinalysis and endocrinology over the study period, no significant changes were observed except for prolactin increased as stated above.

In body weight, blood pressure, pulse rate and temperature over the study period, no clinically significant changes were observed. As adverse events, "weight increased" in 1 subject (1 event), "orthostatic hypotension" in 2 subjects (2 events), and "hypertension" and "hypotension" in 1 subject (1 event) each were reported.

In the mean value of each ECG parameter showed a small change from baseline regardless of the group. There was no subject whose abnormal finding changed from "absent" to "present" between before and after treatment in any group. As an adverse event,

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"electrocardiogram QT prolonged" in 1 subject (1 event) was reported.
Based on the above, after 4 injections of paliperidone palmitate (150 mg in the deltoid muscle, 75 mg in the deltoid muscle and, 75 mg in the gluteal muscle) in schizophrenic patients, the incidence of adverse events, particularly, the incidence of injection site reaction-related adverse events tended to be lower and the number of events was fewer in gluteal injection than in the deltoid injection. The tolerability was good, regardless of the dosage and injection site. The safety profiles observed in this study were consisted with the results of clinical studies conducted in Japan and overseas to date.

Efficacy results:
To patients with schizophrenia, 4 injections (1 injection each on Days 1, 8, 36 and 64) of paliperidone palmitate were administered in the deltoid muscle at 150 mg e.q., in the deltoid and gluteal muscle at 75 mg e.q. to assess the efficacy based on PANSS and CGI-S.
Of the enrolled 80 subjects, 76 subjects received study treatment in this study. After the start of treatment, the following subjects discontinued the study: 8 subjects due to withdrawal of consent, 4 subjects due to adverse events, and 1 subject due to exacerbation of the symptom. As for discontinuation by time, 7 of the 13 discontinued subjects had discontinued the study by Day 36 (before the third study treatment). As a result, 63 subjects completed the study, and the details were 21 subjects in the 150 mg eq./deltoid group, 20 subjects in the 75 mg eq./deltoid group and 22 subjects in the 75 mg eq./gluteal group.
PPS was employed as a primary analysis set for efficacy, and all the 76 subjects treated with the study drug (150 mg eq./deltoid group 24 subjects, 75 mg eq./deltoid group 27 subjects, 75 mg eq./gluteal group 25 subjects) were considered the subjects. The results in [PPS-LOCF] are described below.
PANSS total scores [mean (SD)] at baseline were 66.0 (17.48) in the 150 mg eq./deltoid group, 63.0 (16.68) in the 75 mg eq./deltoid group and 72.1 (19.01) in the 75 mg eq./gluteal

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group. The changes from baseline (least squares mean [95% CI]) in PANSS total score on Day 92 (at the final evaluation) were -3.3 [-8.15; 1.56] in the 150 mg eq./deltoid group, 1.8 [-2.84; 6.39] in the 75 mg eq./deltoid group and -2.2 [-7.01; 2.63] in the 75 mg eq./gluteal group. PANSS total score did not show significant changes from baseline over the observation period in any group, suggesting that the therapeutic efficacy of the study treatment was comparable to those of prior medications.

The proportions of "Mild" or better in CGI-S assessment at baseline were 41.7% (10/24 subjects) in the 150 mg eq./deltoid group, 63.0% (17/27 subjects) in the 75 mg eq./deltoid group and 44.0% (11/25 subjects) in the 75 mg eq./gluteal group. On Day 92 (at the final evaluation), the proportions were 50.0% (12/24 subjects) in the 150 mg eq./deltoid group, 59.3% (16/27 subjects) in the 75 mg eq./deltoid group and 48.0% (12/25 subjects) in the 75 mg eq./gluteal group, and there was no significant change in the proportion over the observation period in any group. The results supported the results in PANSS total score.

In summary, after 4 injections of paliperidone palmitate 150 mg in the deltoid muscle and 75 mg in the deltoid or gluteal muscle in patients with schizophrenia, the efficacy evaluation based on PANSS and CGI-S suggested that the therapeutic efficacy of the study treatment was comparable to those of prior medications.

Name of Sponsor/Company Janssen Pharmaceutical K.K.	Individual Study Table Referring to Part of the Dossier Volume: Page:	(For National Authority Use Only)
Name of Finished Product: To be determined.		
Name of Active Ingredient: Paliperidone		
Date of report: October 27, 2010		

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