Clinical trial results:
Single-arm, Open-label Extension to a Double-blind, Randomized, Active-controlled, Parallel-group Study of Paliperidone Palmitate 6-Month Formulation

Summary

EudraCT number	2018-004532-30
Trial protocol	PL IT
Global end of trial date	03 May 2022

Results information

Result version number	v1 (current)
This version publication date	19 May 2023
First version publication date	19 May 2023

Trial information

Trial identification

Sponsor protocol code	R092670PSY3016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04072575
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 US Highway 202, Raritan, United States, 08869-1420
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to assess (in a limited number of countries) the long-term safety and tolerability of paliperidone palmitate 6-month (PP6M; 700 or 1000 milligrams equivalent [mg eq.]) and to provide access to PP6M in subjects with schizophrenia who completed study R092670PSY3015 (2017-001941-28) without relapse.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 46
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Poland: 44
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	Ukraine: 42
Worldwide total number of subjects	178
EEA total number of subjects	50

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	176
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 178 subjects who completed the 12-month double-blind (DB) phase of study R092670PSY3015 (2017-001941-28) without a relapse, were enrolled in this open-label extension (OLE) study. Out of 178 subjects, 154 completed this OLE study.

Period 1

Period 1 title	Open-label Extention (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.

Arm description:

Subjects who completed the 12-month double-blind (DB) phase of study R092670PSY3015 (2017-001941-28) without a relapse, were enrolled in this open-label extension (OLE) study and received intramuscular (IM) injections of PP6M 700 (if received moderate dose previously) or 1000 milligrams equivalent (mg eq.) (if received higher dose previously) on Day 1. On Days 183, 365, and 547, flexible dosings were permitted to increase PP6M 700 mg eq. to 1000 mg eq. or decrease 1000 mg eq. to 700 mg eq. as per investigator's judgement.

Arm type	Experimental
Investigational medicinal product name	PP6M
Investigational medicinal product code	
Other name	R092670
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

PP6M 700 or 1000 mg eq. IM injections were administered on Days 1, 183, 365, and 547.

Number of subjects in period 1	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.
Started	178
Completed	154
Not completed	24
Physician decision	1
Consent withdrawn by subject	14
Adverse event, non-fatal	7
Unspecified	2

Baseline characteristics

Reporting groups	
Reporting group title	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.

Reporting group description:

Subjects who completed the 12-month double-blind (DB) phase of study R092670PSY3015 (2017-001941-28) without a relapse, were enrolled in this open-label extension (OLE) study and received intramuscular (IM) injections of PP6M 700 (if received moderate dose previously) or 1000 milligrams equivalent (mg eq.) (if received higher dose previously) on Day 1. On Days 183, 365, and 547, flexible dosings were permitted to increase PP6M 700 mg eq. to 1000 mg eq. or decrease 1000 mg eq. to 700 mg eq. as per investigator's judgement.

Reporting group values	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.	Total	
Number of subjects	178	178	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	176	176	
From 65 to 84 years	2	2	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	40.4		
standard deviation	± 10.76	-	
Title for Gender Units: subjects			
Female	52	52	
Male	126	126	

End points

End points reporting groups

Reporting group title	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.

Reporting group description:

Subjects who completed the 12-month double-blind (DB) phase of study R092670PSY3015 (2017-001941-28) without a relapse, were enrolled in this open-label extension (OLE) study and received intramuscular (IM) injections of PP6M 700 (if received moderate dose previously) or 1000 milligrams equivalent (mg eq.) (if received higher dose previously) on Day 1. On Days 183, 365, and 547, flexible dosings were permitted to increase PP6M 700 mg eq. to 1000 mg eq. or decrease 1000 mg eq. to 700 mg eq. as per investigator's judgement.

Primary: Number of Subjects With Relapse

End point title	Number of Subjects With Relapse[1]

End point description:

Number of subjects with relapse were reported. Relapse is defined as one or more of the following: a) Psychiatric hospitalization for schizophrenia (involuntary or voluntary admission to a psychiatric hospital for decompensation of the subject’s schizophrenic symptoms); b) Emergency Department/Room/Ward visit due to a worsening of the subject’s symptoms of schizophrenia, but a psychiatric hospitalization does not occur; c) The subject inflicts deliberate self-injury or exhibits violent behaviour resulting in suicide, clinically significant injury to him/herself or another person, or significant property damage; d) The subject has suicidal or homicidal ideation and aggressive behaviour that is clinically significant (in frequency and severity) in the investigator’s judgment. The intent-to-treat (ITT) analysis population included all subjects who received at least 1 dose of study drug in this study.

End point type	Primary

End point timeframe:

Up to Day 730

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned. No inferential statistics were planned.

End point values	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.			
Subject group type	Reporting group			
Number of subjects analysed	178			
Units: Subjects	7			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)[2]

End point description:

An AE is any untoward medical occurrence in a subject participating in a clinical study that does not

necessarily have a causal relationship with the pharmaceutical/ biological agent under study. TEAEs are those events if they started after administration of the first dose and until 183 days after the last dose of study medication. The safety analysis population included all subjects who received at least 1 dose of study drug in this study.

End point type	Primary

End point timeframe:

Up to Day 730

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were planned. No inferential statistics were planned.

End point values	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.			
Subject group type	Reporting group			
Number of subjects analysed	178			
Units: Subjects	111			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression-Severity (CGI-S) Scale Score

End point title	Change from Baseline in Clinical Global Impression-Severity (CGI-S) Scale Score

End point description:

Change from baseline in CGI-S scale score was reported. CGI-S is defined as clinician-rated scale that assesses the severity of mental illness on a scale of 0 to 7. Considering total clinical experience, a subject was assessed on severity of mental illness at the time of rating according to:1: normal, not at all ill; 2: borderline mentally ill; 3: mildly ill; 4: moderately ill; 5: markedly ill; 6: severely ill; 7: among the most extremely ill subjects. A higher score implies a more severe condition. The ITT analysis population included all subjects who received at least 1 dose of study drug in this study. Here, 'N' (number of subjects analysed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 730

End point values	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: Units on a scale				
arithmetic mean (standard deviation)	0.0 (± 0.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Personal and Social Performance (PSP) Scale Score

End point title	Change from Baseline in Personal and Social Performance (PSP) Scale Score

End point description:

Change from baseline in PSP scale score was reported. The PSP scale assesses degree of a subject's dysfunction within 4 domains of behavior: 1) socially useful activities, 2) personal and social relationships, 3) self-care, and 4) disturbing and aggressive behavior. Each domain was assessed on a 6-point scale, from 1 (absent) to 6 (very severe) (1 = absent, 2 = mild, 3 = manifest, 4 = marked, 5 = severe, and 6 = very severe). PSP total score was calculated as sum of all the domain scores and ranges from 1 to 100. Subjects with score of 71 to 100 had mild degree of difficulty; from 31 to 70, varying degrees of disability; less than or equal to 30, functioning so poorly as to require intensive supervision. Higher score indicates better performance. The ITT analysis population included all subjects who received at least 1 dose of study drug in this study. Here, 'N' (number of subjects analysed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 730

End point values	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: Units on a scale				
arithmetic mean (standard deviation)	0.5 (± 7.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score

End point title	Change from Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score

End point description:

Change from baseline in PANSS total score were reported. The neuropsychiatric symptoms of schizophrenia were assessed using the 30-item PANSS scale, which provides a total score (sum of the

scores for all 30 items) and scores for 3 subscales: the 7-item positive-symptom (P) subscale, the 7-item negative-symptom (N) subscale, and the 16-item general-psychopathology symptom (G) subscale. Each item is rated on a scale of 1 (absent) to 7 (extreme). The PANSS total score ranges from 30 (absent disease)-210 (more severe neuropsychiatric symptoms of schizophrenia). The ITT analysis population included all subjects who received at least 1 dose of study drug in this study. Here, 'N' (number of subjects analysed) signifies subjects evaluated for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 730

End point values	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: Units on a scale				
arithmetic mean (standard deviation)	0.7 (± 8.22)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 730

Adverse event reporting additional description:

The safety analysis population included all subjects who received at least 1 dose of study drug in this study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.

Reporting group description:

Subjects who completed the 12-month double-blind (DB) phase of study R092670PSY3015 (2017-001941-28) without a relapse, were enrolled in this open-label extension (OLE) study and received intramuscular (IM) injections of PP6M 700 (if received moderate dose previously) or 1000 milligrams equivalent (mg eq.) (if received higher dose previously) on Day 1. On Days 183, 365, and 547, flexible dosings were permitted to increase PP6M 700 mg eq. to 1000 mg eq. or decrease 1000 mg eq. to 700 mg eq. as per investigator's judgement.

Serious adverse events	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 178 (4.49%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon Cancer			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to Peritoneum			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrotic Syndrome			

subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychiatric Symptom			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			
subjects affected / exposed	4 / 178 (2.25%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Hallucination, Auditory			
subjects affected / exposed	1 / 178 (0.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Total Paliperidone Palmitate 6-month (PP6M) 700 or 1000 mg eq.		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 178 (38.20%)		
Investigations			
Weight Increased			
subjects affected / exposed	9 / 178 (5.06%)		
occurrences (all)	9		
Blood Prolactin Increased			
subjects affected / exposed	19 / 178 (10.67%)		
occurrences (all)	19		
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 178 (13.48%)		
occurrences (all)	30		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	11 / 178 (6.18%) 12		
Endocrine disorders Hyperprolactinaemia subjects affected / exposed occurrences (all)	13 / 178 (7.30%) 13		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 178 (5.06%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2020	The overall rational of this amendment was to remove text related to anticipated events which do not apply in single arm open-label extension study and to increase the estimated number of subjects to be enrolled in the study for multiple reasons relating to preceding double-blind study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The sponsor identified that the study did not include a control arm reference group. The coronavirus disease-2019 (COVID-19) pandemic placed some restrictions on study face-to-face visits.

Notes: