Clinical trial results:
A 52-Week, Open-Label, Extension Study of Pimavanserin for the Adjunctive Treatment of Schizophrenia

Summary

EudraCT number	2016-003435-38
Trial protocol	HU ES BG CZ DE LT PL IT HR
Global end of trial date	30 May 2024

Results information

Result version number	v1 (current)
This version publication date	30 May 2025
First version publication date	30 May 2025

Trial information

Trial identification

Sponsor protocol code	ACP-103-035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03121586
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Acadia Pharmaceuticals Inc.
Sponsor organisation address	12830 El Camino Real, Suite 400, San Diego, United States, 92130
Public contact	Sr. Dir. Medical Information and Medical Communications, ACADIA Pharmaceuticals Inc., 1 58261 2897, medicalinformation@acadia-pharm.com
Scientific contact	Sr. Dir. Medical Information and Medical Communications, ACADIA Pharmaceuticals Inc., 1 58261 2897, medicalinformation@acadia-pharm.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	30 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2024
Global end of trial reached?	Yes
Global end of trial date	30 May 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of pimavanserin after 52 weeks of adjunctive treatment in subjects with schizophrenia

Protection of trial subjects:

Not applicable

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	18 January 2017
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	Poland: 13
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	Croatia: 10
Country: Number of subjects enrolled	Bulgaria: 281
Country: Number of subjects enrolled	Czechia: 25
Country: Number of subjects enrolled	Hungary: 27
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Lithuania: 9
Country: Number of subjects enrolled	Argentina: 63
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Russian Federation: 214
Country: Number of subjects enrolled	Serbia: 162
Country: Number of subjects enrolled	Ukraine: 93
Country: Number of subjects enrolled	United States: 72
Worldwide total number of subjects	995
EEA total number of subjects	389

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)	995
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label extension study for patients from studies ACP-103-034, 038, and 064. Patients who had completed any of those studies and had not shown significant worsening of symptoms, or who may have benefited, or were expected to benefit from continued pimavanserin treatment based on the investigator's judgment were eligible.

Pre-assignment

Screening details:

Informed consent was obtained before the final procedures of each study, performed at Week 6 for study 034 and Week 26 for studies 038 and 064. Procedures performed at the end of study visits of the 3 double-blind studies were carried over to study 035 and were used baseline information; the respective visits were considered as baseline visit.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Pimavanserin

Arm description:

Pimavanserin once daily administered orally

Arm type	Experimental
Investigational medicinal product name	Pimavanserin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pimavanserin once daily administered orally.
Patients rolling over from studies ACP-103-034 or ACP-103-038 received pimavanserin 20 mg for the first 2 weeks. Thereafter, the daily dose could be adjusted to 34, 20, or 10 mg throughout the study, based on the investigator's assessment of clinical response in the individual patient. Dose adjustments were made at scheduled or unscheduled visits.
Patients rolling over from study ACP-103-064 received pimavanserin 34 mg throughout the entire treatment duration.

Number of subjects in period 1	Pimavanserin
Started	995
Completed	745
Not completed	250
Adverse event, serious fatal	2
Consent withdrawn by subject	60
Physician decision	4

Adverse event, non-fatal	27
Study terminated by sponsor	99
Noncompliance with study drug	13
Lost to follow-up	6
Not further specified	27
Protocol deviation	5
Lack of efficacy	7

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	995	995	
Age categorical Units: Subjects			
Adults (18-64 years)	995	995	
Age continuous Units: years arithmetic mean standard deviation	 37.7 ± 9.36	 -	
Gender categorical Units: Subjects			
Female	370	370	
Male	625	625	

End points

End points reporting groups

Reporting group title	Pimavanserin

Reporting group description:

Pimavanserin once daily administered orally

Primary: Number of Patients With Treatment Emergent Adverse Events

End point title	Number of Patients With Treatment Emergent Adverse

End point description:

End point type	Primary

End point timeframe:

Treatment period (52 weeks) and follow-up period (30 days): planned total of 56 weeks. As the study was prematurely terminated, the reporting period was shortened; AEs were assessed to the end of treatment, at a mean duration of 319 days (or 46 weeks).

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: This was an open-label, uncontrolled extension study. The study had no primary efficacy endpoint; the primary endpoint was safety-related. Inferential statistics were neither planned nor performed for this endpoint.

End point values	Pimavanserin			
Subject group type	Reporting group			
Number of subjects analysed	955			
Units: Patients	349			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment period (52 weeks) and follow-up period (30 days): planned total of 56 weeks. As the study was prematurely terminated, the reporting period was shortened; AEs were assessed to the end of treatment, at a mean duration of 319 days (or 46 weeks).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Pimavanserin

Reporting group description: -

Serious adverse events	Pimavanserin		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 995 (2.11%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tongue neoplasm benign			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drowning				
subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Dental cyst				
subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Completed suicide				
subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric decompensation				
subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Schizophrenia				
subjects affected / exposed	7 / 995 (0.70%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 0			
Substance-induced psychotic disorder				
subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	1 / 995 (0.10%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 995 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 995 (0.10%)		
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	Pimavanserin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 995 (7.04%)		
Nervous system disorders			
Headache			
subjects affected / exposed	70 / 995 (7.04%)		
occurrences (all)	83		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2016	- Added as secondary objective to characterise the pharmacokinetics and pharmacodynamics of pimavanserin in the study population - Increased the number of study sites from 100 to 160 - Removed abstinence as a clinically acceptable method of contraception - Revised Exclusion Criterion 11 from "a history of suicide attempt, actively suicidal, at imminent risk of self-harm, or answers yes to 4 or 5 on the C-SSRS in Studies 034, 038, or 039" to "is at a significant risk of suicide or is a danger to self or others in the opinion of the Investigator" - Revised test product, dose, and administration details from two 10 mg tablets once daily to 10 mg and 17 mg tablets to be provided as one 10 mg tablet, two 10 mg tablets, or two 17 mg tablets - Added PK sampling for patients who experienced an SAE or AE leading to discontinuation - Added details for PK and PK/PD analyses - Added section for reporting on overdose of study drug - Updated prohibited and concomitant medications
31 March 2017	- Removed PK objectives and assessments for business reasons and to reduce patient burden - Modified inclusion and exclusion criteria to better reflect the targeted patient population - Clarified the AE reporting period and related SAE reporting - Modified exclusion criteria related to urine drug screen and long QT syndrome
11 August 2020	- Replaced study ACP-103-039 with study ACP-103-064 as parent study from which patients could roll over to the present study and implemented protocol changes to align with incorporation of study ACP-103-064 patients (in terms of dosing regimen; secondary and exploratory endpoints; safety related exclusion criteria) – Prohibited subjects from Study 064 with positive marijuana test from participating - Revised study indication from "schizophrenia" to "negative symptoms of schizophrenia" - Added paliperidone extended release and paliperidone palmitate to the list of main antipsychotics - Aligned with changes from previous local amendment (Amendment 2-CZ) to generate a single global protocol amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 April 2024	The study was terminated prematurely by the sponsor for business reasons.	-

Notes:

Limitations and caveats

None reported