



Clinical trial results:

A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Pimavanserin for the Treatment of Irritability Associated With Autism Spectrum Disorder

Summary

EudraCT number	2021-005387-22
Trial protocol	ES FR HU PL IT
Global end of trial date	29 August 2024

Results information

Result version number	v1 (current)
This version publication date	10 August 2025
First version publication date	10 August 2025

Trial information

Trial identification

Sponsor protocol code	ACP-103-069
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05523895
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., 001 8582612897, medicalinformation@acadia-pharm.com
Scientific contact	Sr. Dir. Medical Information and Medical Communications, Acadia Pharmaceuticals Inc., 001 8582612897, 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	29 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 August 2024
Global end of trial reached?	Yes
Global end of trial date	29 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of pimavanserin compared with placebo in the treatment of irritability associated with ASD in children and adolescents

Protection of trial subjects:

Not applicable

Background therapy:

No

Evidence for comparator: -

Actual start date of recruitment	16 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	United States: 117
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Serbia: 11
Country: Number of subjects enrolled	Poland: 58
Worldwide total number of subjects	237
EEA total number of subjects	102

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)	167
Adolescents (12-17 years)	70
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening period, patients were assessed for study eligibility, the ability to swallow a test capsule (i.e. placebo), and prohibited medications were discontinued if medically appropriate.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Pimavanserin-matching placebo, given as 1 capsule once daily

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule once daily

Arm title	Pimavanserin Low Dose
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Arm description:

Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 10 mg/day; patients aged 13-17 years: 20 mg/day

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

Dosage and administration details:

Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 10 mg/day; patients aged 13-17 years: 20 mg/day

Arm title	Pimavanserin High Dose
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Arm description:

Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 20 mg/day; patients aged 13-17 years: 34 mg/day

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

Dosage and administration details:

Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 20 mg/day; patients aged 13-17 years: 34 mg/day

Number of subjects in period 1	Placebo	Pimavanserin Low Dose	Pimavanserin High Dose
Started	78	78	81
Completed	74	67	75
Not completed	4	11	6
Consent withdrawn by subject	1	3	1
Adverse event, non-fatal	2	1	1
Noncompliance with study drug	1	1	1
Lost to follow-up	-	1	2
Not further specified	-	3	1
Protocol deviation	-	2	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Pimavanserin-matching placebo, given as 1 capsule once daily	
Reporting group title	Pimavanserin Low Dose
Reporting group description: Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 10 mg/day; patients aged 13-17 years: 20 mg/day	
Reporting group title	Pimavanserin High Dose
Reporting group description: Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 20 mg/day; patients aged 13-17 years: 34 mg/day	

Reporting group values	Placebo	Pimavanserin Low Dose	Pimavanserin High Dose
Number of subjects	78	78	81
Age categorical Units: Subjects			
Children (2-11 years)	53	57	57
Adolescents (12-17 years)	25	21	24
Age continuous Units: years			
arithmetic mean	9.8	9.8	9.8
standard deviation	± 2.88	± 3.54	± 3.11
Gender categorical Units: Subjects			
Female	21	19	13
Male	57	59	68

Reporting group values	Total		
Number of subjects	237		
Age categorical Units: Subjects			
Children (2-11 years)	167		
Adolescents (12-17 years)	70		
Age continuous Units: years			
arithmetic mean	-		
standard deviation	-		
Gender categorical Units: Subjects			
Female	53		
Male	184		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Pimavanserin-matching placebo, given as 1 capsule once daily	
Reporting group title	Pimavanserin Low Dose
Reporting group description: Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 10 mg/day; patients aged 13-17 years: 20 mg/day	
Reporting group title	Pimavanserin High Dose
Reporting group description: Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 20 mg/day; patients aged 13-17 years: 34 mg/day	

Primary: Change From Baseline at Week 6 in Caregiver-rated Aberrant Behavior Checklist (ABC) Irritability Subscale Score

End point title	Change From Baseline at Week 6 in Caregiver-rated Aberrant Behavior Checklist (ABC) Irritability Subscale Score
End point description: The Aberrant Behavior Checklist (ABC) is a caregiver-rated scale comprised of 5 empirically-derived subscales encompassing 58 items that describe various behavior problems. It measures domains of irritability, lethargy/social withdrawal, stereotypic behavior, hyperactivity/noncompliance, and inappropriate speech. ABC-Irritability is one of the subscales and comprises of 15 items. Minimum score is 0, maximum is 45. A score for each item ranges from 0 indicating "not at all a problem" to 3 indicating "the problem is severe in degree". Subscale scores are calculated by summing the items within that subscale. Higher scores indicate greater impairment.	
End point type	Primary
End point timeframe: 6 weeks	

End point values	Placebo	Pimavanserin Low Dose	Pimavanserin High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	64	74	
Units: Score on a scale				
least squares mean (standard error)	-9.6 (± 1.06)	-11.2 (± 1.09)	-11.2 (± 1.05)	

Statistical analyses

Statistical analysis title	Placebo vs Pimavanserin Low Dose
Comparison groups	Placebo v Pimavanserin Low Dose

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2986
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	1.52

Statistical analysis title	Placebo vs Pimavanserin High Dose
Comparison groups	Placebo v Pimavanserin High Dose
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2859
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	1.49

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening to end of safety follow-up, which was to be performed at 10 weeks, i.e. 4 weeks after last dose of study drug.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Pimavanserin-matching placebo, given as 1 capsule once daily

Reporting group title	Pimavanserin Low Dose
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Reporting group description:

Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 10 mg/day; patients aged 13-17 years: 20 mg/day

Reporting group title	Pimavanserin High Dose
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Reporting group description:

Pimavanserin given as 1 capsule once daily. Patients aged 5-12 years: 20 mg/day; patients aged 13-17 years: 34 mg/day

Serious adverse events	Placebo	Pimavanserin Low Dose	Pimavanserin High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 78 (1.28%)	0 / 77 (0.00%)	0 / 81 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 78 (1.28%)	0 / 77 (0.00%)	0 / 81 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Pimavanserin Low Dose	Pimavanserin High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 78 (14.10%)	17 / 77 (22.08%)	16 / 81 (19.75%)
Nervous system disorders			

Headache			
subjects affected / exposed	4 / 78 (5.13%)	5 / 77 (6.49%)	5 / 81 (6.17%)
occurrences (all)	4	5	6
Somnolence			
subjects affected / exposed	4 / 78 (5.13%)	2 / 77 (2.60%)	4 / 81 (4.94%)
occurrences (all)	4	3	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 78 (1.28%)	4 / 77 (5.19%)	1 / 81 (1.23%)
occurrences (all)	1	6	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 78 (5.13%)	7 / 77 (9.09%)	5 / 81 (6.17%)
occurrences (all)	4	7	6
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 78 (0.00%)	4 / 77 (5.19%)	2 / 81 (2.47%)
occurrences (all)	0	4	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 April 2021	- Increased the sample size from approx. 300 patients screened/180 randomized to approx. 380 patients screened/ 228 randomized; increased the number of sites to 60. - Indicated that mild sedation was to only be used in exceptional circumstances and that involvement of experienced personnel in the conduction of routine procedures was strongly recommended - Indicated that the Investigator was solely responsible for final decisions concerning subject eligibility - Clarified language concerning sparse PK sampling, certain inclusion/ exclusion criteria, remote visits, patient discontinuation and withdrawal, and time period when medication prohibitions applied - Stipulated that prolactin results remained blinded to investigator and sponsor (but was monitored independently by the CRO) - Reduced the recallperiod for the Caregiver Strain Questionnaire consistent with the time frame of the study - Added COVID-19 vaccination history or occurrence to assessments - Added pregnancy test at Week 3 - Adjusted contraceptive language to make it appropriate for premenarchal subjects - Defined caregivers allowed to provide input for caregiver-facing scales, and indicated that caregivers were trained in accurate symptom reporting for the ABC, Repetitive Behavior Scale-Revised, and CGSQ scales - Indicated that vital signs were optional at remote visits - Made the Week 4 visit an in-clinic visit with study drug dispensation - Added lorazepam as rescue medication
03 December 2021	- Indicated that height, weight, and BMI measurements were optional at remote visits - Indicated that it is the sponsor/Medical Monitor who decides whether a patient who had taken prohibited medication continues in the trial - Added informed consent of a non-parent/LAR caregiver to the inclusion criteria and clarified informed consent language - Indicated that every attempt will be made to recruit equal numbers of patients from both age groups - Clarified inclusion criterion #8 so that patients will be screenfailures instead of withdrawn from the study if their ABC-I score at baseline exceeds $\geq 20\%$ improvement from tje screening value - Clarified language relating to prior antipsychotic treatment - Adjusted exclusion criterion #16 to include blood pressure limits appropriate for both age groups - Removed physical examination from unscheduled visits - Updated the list of prohibited medications

25 March 2022	- Specified that AEs of syncope and somnolence are actively monitored at each visit and that pertinent information was to be collected also as part of medical history - Adjusted exclusion criteria for blood pressure such that they were age-specific - Added stratification by geographic region (US versus rest of world) - Specified extension of the open-label extension study from 26 weeks to 52 weeks - Indicated that height should be measured using a stadiometer - Increased the frequency of ESRS-A assessments (to be conducted at all clinic visits) - Specified that all known potential class side effects of antipsychotics will be actively monitored - Added to the protocol appendix criteria for potentially clinically important laboratory values, ECG values, and vital signs - Specified that for patients reporting symptoms of orthostatic hypotension, this should be specifically measured - Specified that HbA1c was to be measured at all visits
21 December 2022	- Allowed inclusion of patients on stable doses of stimulants and non-stimulants targeting irritability into the study - Provided flexibility in the timing of screening assessments, use of local laboratories, remote assessments, and conduct of the Autism Diagnostic Interview-Revised - Allowed for the capsule swallowing test to be passed either at screening or baseline - Adjusted the number of patients screened in the light of the higher-than-expected screen failure rate experienced in the study - Standardised washout periods to 5 half-lives or 2 weeks, whichever is longer - Removed the exclusion criterion regarding premature ventricular contractions (PVCs) - Updated the list of CYP3A4 inhibitors and inducers as per the FDA website

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.

Not applicable

Notes: