



Clinical trial results:

A multi-center, open-label extension study to examine the safety and tolerability of ACP-103 in the treatment of psychosis in Parkinson's Disease

Summary

EudraCT number	2007-003035-22
Trial protocol	GB FR SE BE AT PT IT
Global end of trial date	30 May 2018

Results information

Result version number	v1 (current)
This version publication date	14 June 2019
First version publication date	14 June 2019

Trial information

Trial identification

Sponsor protocol code	ACP-103-015
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00550238
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ACADIA Pharmaceuticals Inc.
Sponsor organisation address	3611 Valley Centre Drive, Ste. 300, San Diego, CA, United States, 92130
Public contact	Sr. Dir. Medical Information and Medical Communications, ACADIA Pharmaceuticals Inc., +1 858-261-2897, medicalinformation@acadia-pharm.com
Scientific contact	Sr. Dir. Medical Information and Medical Communications, ACADIA Pharmaceuticals Inc., +1 858-261-2897, 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 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2018
Global end of trial reached?	Yes
Global end of trial date	30 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and tolerability of ACP-103 in patients with Parkinson's Disease Psychosis (PDP)

This study did not have a fixed duration, and the duration of individual patient participation was determined based on investigator assessment of patient tolerability and continued benefit until such time as either the drug was commercially available in the US, or an alternate treatment extension was available in non-US regions. For this reason, no patients, therefore, were considered to have "completed" the study.

Protection of trial subjects:

Not applicable

Background therapy:

Patients were allowed to continue protocol-permitted medications

Evidence for comparator:

Not applicable; this was a single-arm, uncontrolled study.

Actual start date of recruitment	26 July 2007
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: 3
Country: Number of subjects enrolled	Portugal: 10
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	India: 18
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	Serbia: 12
Country: Number of subjects enrolled	Ukraine: 22
Country: Number of subjects enrolled	United States: 317

Worldwide total number of subjects	459
EEA total number of subjects	48

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)	90
From 65 to 84 years	355
85 years and over	14

Subject disposition

Recruitment

Recruitment details:

Eligible patients were adult males or females with Parkinson's Disease Psychosis who had completed a prior double blind study with pimavanserin and were determined by the treating physician (Investigator) to benefit from continued treatment. This study did not have a fixed duration. Thus, no patients were considered to have "completed" the study.

Pre-assignment

Screening details:

Patients could be enrolled in this study as early as the final visit of the previous double-blind study, or up to 28 days following completion of the treatment period of the previous double-blind study.

Period 1

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

Arms

Arm title	Pimavanserin
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Arm description:

Pimavanserin tartrate (ACP-103) tablets taken once daily by mouth for as long as the drug is considered to be tolerated and beneficial to patients

Arm type	Experimental
Investigational medicinal product name	Pimavanserin
Investigational medicinal product code	ACP-103
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Pimavanserin 40 mg (2 x 20 mg tablets, given as pimavanserin Tartrate) administered once daily by mouth.

Number of subjects in period 1	Pimavanserin
Started	459
Completed	0
Not completed	459
Adverse event, serious fatal	34
Consent withdrawn by subject	167
Physician decision	31
Disease progression	46
Adverse event, non-fatal	88
Patient noncompliance	25
Lost to follow-up	13
Sponsor decision	55

Baseline characteristics

Reporting groups

Reporting group title	Pimavanserin
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Reporting group description:

Pimavanserin tartrate (ACP-103) tablets taken once daily by mouth for as long as the drug is considered to be tolerated and beneficial to patients

Reporting group values	Pimavanserin	Total	
Number of subjects	459	459	
Age categorical			
Units: Subjects			
Adults (18-64 years)	90	90	
From 65-84 years	355	355	
85 years and over	14	14	
Age continuous			
Units: years			
arithmetic mean	71.2		
standard deviation	± 8.19	-	
Gender categorical			
Units: Subjects			
Female	176	176	
Male	283	283	

End points

End points reporting groups

Reporting group title	Pimavanserin
Reporting group description: Pimavanserin tartrate (ACP-103) tablets taken once daily by mouth for as long as the drug is considered to be tolerated and beneficial to patients	

Primary: Number (%) of patients with drug-related treatment-emergent adverse events (AEs)

End point title	Number (%) of patients with drug-related treatment-emergent adverse events (AEs) ^[1]
End point description: Number (%) of patients with drug-related treatment-emergent AEs (i.e. AEs reported by the Investigator as possibly, probably, or highly probably related to study drug)	
End point type	Primary
End point timeframe: From first to last study drug dose plus 30 days	

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 a single-arm, uncontrolled trial. The primary endpoint was analysed using descriptive statistics only. No inferential testing was applied. A p-value was not defined.

End point values	Pimavanserin			
Subject group type	Reporting group			
Number of subjects analysed	459 ^[2]			
Units: Patients	180			

Notes:

[2] - Enrolled patients who received at least 1 dose of study drug

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first to last study drug dose plus 30 days

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	Pimavanserin
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Reporting group description:

Pimavanserin tartrate (ACP-103) tablets taken once daily by mouth for as long as the drug is considered to be tolerated and beneficial to patients

Serious adverse events	Pimavanserin		
Total subjects affected by serious adverse events			
subjects affected / exposed	188 / 459 (40.96%)		
number of deaths (all causes)	59		
number of deaths resulting from adverse events	59		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	3 / 459 (0.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Bladder cancer			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain neoplasm			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Colon cancer stage III			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hepatic neoplasm malignant			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Meningioma benign			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple myeloma			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraproteinaemia			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Recurrent cancer			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	5 / 459 (1.09%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	4 / 459 (0.87%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Aortic aneurysm			

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Aortic dissection			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Circulatory collapse			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypertensive crisis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Deep brain stimulation			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin neoplasm excision			
subjects affected / exposed	1 / 459 (0.22%)		
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	6 / 459 (1.31%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		

Death				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 2			
Asthenia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Axillary pain				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inflammation				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vaginal prolapse				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	11 / 459 (2.40%)		
occurrences causally related to treatment / all	1 / 13		
deaths causally related to treatment / all	1 / 2		
Pulmonary embolism			
subjects affected / exposed	8 / 459 (1.74%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	5 / 459 (1.09%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 4		
Respiratory failure			
subjects affected / exposed	3 / 459 (0.65%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 2		
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Aspiration			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Atelectasis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Atypical pneumonia			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Choking			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydropneumothorax			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory distress			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	7 / 459 (1.53%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			

subjects affected / exposed	7 / 459 (1.53%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	6 / 459 (1.31%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Hallucination, visual				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Abnormal behaviour				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aggression				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Delusion				

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jealous delusion			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Panic attack			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Nuclear magnetic resonance imaging			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	10 / 459 (2.18%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	6 / 459 (1.31%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		

Femoral neck fracture				
subjects affected / exposed	4 / 459 (0.87%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Craniocerebral injury				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Laceration				

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural complication			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue injury			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stress fracture			

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Thoracic vertebral fracture			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxicity to various agents			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	4 / 459 (0.87%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	5 / 459 (1.09%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 3		
Cardiac arrest			
subjects affected / exposed	3 / 459 (0.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Cardiac failure congestive			
subjects affected / exposed	3 / 459 (0.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Angina pectoris			

subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Cardio-respiratory arrest				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Cardiopulmonary failure				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Coronary artery disease				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Atrial flutter				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial ischaemia			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sick sinus syndrome			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Parkinson's disease			
subjects affected / exposed	10 / 459 (2.18%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 5		
Syncope			
subjects affected / exposed	8 / 459 (1.74%)		
occurrences causally related to treatment / all	2 / 9		
deaths causally related to treatment / all	0 / 0		
Dementia			
subjects affected / exposed	7 / 459 (1.53%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 3		
Cerebrovascular accident			
subjects affected / exposed	5 / 459 (1.09%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Transient ischaemic attack			

subjects affected / exposed	4 / 459 (0.87%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	3 / 459 (0.65%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	3 / 459 (0.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	3 / 459 (0.65%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Toxic encephalopathy				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Autonomic nervous system imbalance				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Burning sensation				

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Haemorrhagic stroke			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ischaemic stroke			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lethargy			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuroleptic malignant syndrome			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
On and off phenomenon			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Parkinsonism			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Crohn's disease				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyschezia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Faecaloma				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hiatus hernia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Melaena				

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presbyoesophagus			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal prolapse			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bile duct obstruction			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bladder neck obstruction			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Calculus ureteric			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure chronic			

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	4 / 459 (0.87%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	3 / 459 (0.65%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc disorder			
subjects affected / exposed	2 / 459 (0.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Exostosis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteochondrosis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Scoliosis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal column stenosis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spondylolysis			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	21 / 459 (4.58%)		
occurrences causally related to treatment / all	0 / 23		
deaths causally related to treatment / all	0 / 5		
Urinary tract infection			
subjects affected / exposed	17 / 459 (3.70%)		
occurrences causally related to treatment / all	1 / 19		
deaths causally related to treatment / all	0 / 1		
Sepsis			
subjects affected / exposed	7 / 459 (1.53%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
Cellulitis			

subjects affected / exposed	4 / 459 (0.87%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	3 / 459 (0.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	3 / 459 (0.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	3 / 459 (0.65%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Candiduria				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Coccidioidomycosis				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Urosepsis				

subjects affected / exposed	2 / 459 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Abscess limb				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterococcal sepsis				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fungal infection				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	1 / 459 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				

subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	1 / 459 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	9 / 459 (1.96%)		
occurrences causally related to treatment / all	0 / 9		
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	328 / 459 (71.46%)		
Investigations			
Weight decreased			
subjects affected / exposed	57 / 459 (12.42%)		
occurrences (all)	65		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	145 / 459 (31.59%)		
occurrences (all)	326		
Contusion			
subjects affected / exposed	37 / 459 (8.06%)		
occurrences (all)	55		
Laceration			

subjects affected / exposed	36 / 459 (7.84%)		
occurrences (all)	51		
Excoriation			
subjects affected / exposed	23 / 459 (5.01%)		
occurrences (all)	41		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	40 / 459 (8.71%)		
occurrences (all)	48		
Hypertension			
subjects affected / exposed	34 / 459 (7.41%)		
occurrences (all)	36		
Nervous system disorders			
Dizziness			
subjects affected / exposed	43 / 459 (9.37%)		
occurrences (all)	50		
Dementia			
subjects affected / exposed	30 / 459 (6.54%)		
occurrences (all)	33		
Somnolence			
subjects affected / exposed	29 / 459 (6.32%)		
occurrences (all)	33		
Parkinson's disease			
subjects affected / exposed	27 / 459 (5.88%)		
occurrences (all)	30		
Headache			
subjects affected / exposed	23 / 459 (5.01%)		
occurrences (all)	30		
Tremor			
subjects affected / exposed	23 / 459 (5.01%)		
occurrences (all)	26		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	35 / 459 (7.63%)		
occurrences (all)	37		
General disorders and administration site conditions			

Oedema peripheral subjects affected / exposed occurrences (all)	43 / 459 (9.37%) 52		
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	46 / 459 (10.02%) 54		
Dysphagia subjects affected / exposed occurrences (all)	43 / 459 (9.37%) 46		
Nausea subjects affected / exposed occurrences (all)	39 / 459 (8.50%) 49		
Psychiatric disorders			
Hallucination subjects affected / exposed occurrences (all)	62 / 459 (13.51%) 89		
Confusional state subjects affected / exposed occurrences (all)	50 / 459 (10.89%) 65		
Anxiety subjects affected / exposed occurrences (all)	41 / 459 (8.93%) 47		
Depression subjects affected / exposed occurrences (all)	39 / 459 (8.50%) 41		
Insomnia subjects affected / exposed occurrences (all)	34 / 459 (7.41%) 36		
Psychotic disorder subjects affected / exposed occurrences (all)	33 / 459 (7.19%) 39		
Agitation subjects affected / exposed occurrences (all)	32 / 459 (6.97%) 37		
Cognitive disorder			

subjects affected / exposed occurrences (all)	28 / 459 (6.10%) 33		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	31 / 459 (6.75%)		
occurrences (all)	42		
Back pain			
subjects affected / exposed	28 / 459 (6.10%)		
occurrences (all)	38		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	79 / 459 (17.21%)		
occurrences (all)	160		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	25 / 459 (5.45%)		
occurrences (all)	34		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2007	<ul style="list-style-type: none">- Added EudraCT number- Deleted use of a medication diary for recording study drug dosing- Revised schedule of assessments- Added use of a centralized rating Service for conducting SAPS assessment at North American Centers- Replaced Non-Motor Symptoms Questionnaire with the NMSS
30 August 2007	<ul style="list-style-type: none">- Added Exclusion Criterion 2 (failed a prior antipsychotic medication)- Modified Exclusion Criterion 5 (females of nonchildbearing potential)- Replaced centralised ECG reads with Investigator-read ECGs
14 November 2007	<ul style="list-style-type: none">- Deleted Exclusion Criterion 2 (prior antipsychotic medication)- Updated/ corrected SAE reporting procedures- Updated pregnancy reporting procedures
14 April 2008	<ul style="list-style-type: none">- Increased number of study centers from About 100 to 130- Revised Exclusion Criterion 5 (sex-specific QTcB criteria; deleted QRS and PR requirements)- Added: test article description; drug packaging; dosage and administration- Updated sample collection and bioanalytical processing specifications- Replaced pCRFs with eCRFs- Added description of PK Analysis- Added caregiver information in regard to Subject Informed Consent- Specified use of antipsychotics, centrally acting anticholinergics, anticholinesterase inhibitors, amantadine, antidepressants, and anxiolytics- Removed Clinical Global Impression Efficacy Index
04 August 2008	<ul style="list-style-type: none">- Added RUD-Lite, a health economics outcome questionnaire, as an exploratory endpoint
30 June 2010	<ul style="list-style-type: none">- Replaced ACP-103 with pimavanserin- Allowed enrolment of patients with PDP from any double-blind study of pimavanserin- Eliminated Week 1 phone call- Replaced 3-monthly visits (beyond Month 12) by 6-monthly visits- Deleted Inclusion Criterion 2 (stimulator settings for patients that had received stereotaxic surgery for subthalamic nucleus deep brain Stimulation)- Deleted Exclusion Criterion 2 (previous ablative stereotaxic surgery)- Reduced planned patient number from 560 to 400- Increased number of study centers from 130 to 150- Removed NMSS scale

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.

None

Notes: