



Clinical trial results:

A 52-Week Open-Label Extension Study of Pimavanserin in Subjects With Major Depressive Disorder and Inadequate Response to Antidepressant Treatment

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2018-003252-20 |
| Trial protocol | GB SK PL FI |
| Global end of trial date | 22 February 2021 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 08 March 2022 |
| First version publication date | 08 March 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | ACP-103-055 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04000009 |
| 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, +1 858 261 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 | 22 February 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 February 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 February 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of long-term pimavanserin treatment in subjects with major depressive disorder and inadequate response to antidepressant treatment

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment | 06 June 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 | Poland: 16 |
| Country: Number of subjects enrolled | Slovakia: 5 |
| Country: Number of subjects enrolled | United Kingdom: 27 |
| Country: Number of subjects enrolled | Finland: 10 |
| Country: Number of subjects enrolled | Russian Federation: 26 |
| Country: Number of subjects enrolled | Serbia: 13 |
| Country: Number of subjects enrolled | South Africa: 1 |
| Country: Number of subjects enrolled | Ukraine: 26 |
| Country: Number of subjects enrolled | United States: 111 |
| Worldwide total number of subjects | 235 |
| EEA total number of subjects | 31 |

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) | 218 |
| From 65 to 84 years | 17 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study recruited patients that had completed a previous study of pimavanserin, i.e. study ACP-103-054 or ACP-103-059. It was planned to enroll about 420 patients.

The study was terminated early by the Sponsor for business reasons due to the COVID-19 pandemic; there were no safety concerns contributing to study termination.

Pre-assignment

Screening details:

During the screening period, subjects were assessed for study eligibility and prohibited medications were discontinued when medically appropriate.

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 |
|-----------|--------------|

Arm description:

Pimavanserin 34 mg (administered as 2 x 17 mg pimavanserin tablets) once daily, for 52 weeks

| | |
|----------------------------------------|--------------|
| 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 34 mg (administered as 2 x 17 mg pimavanserin tablets) taken once daily, for 52 weeks

| Number of subjects in period 1 | Pimavanserin |
|--------------------------------|--------------|
| Started | 235 |
| Completed | 70 |
| Not completed | 165 |
| Physician decision | 1 |
| Consent withdrawn by subject | 22 |
| Adverse event, non-fatal | 13 |
| Pregnancy | 1 |
| Study terminated by sponsor | 98 |
| Noncompliance with study drug | 4 |
| Use of prohibited medication | 3 |
| Lost to follow-up | 8 |
| Not further specified | 8 |

| | |
|------------------|---|
| Lack of efficacy | 7 |
|------------------|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall study |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | Overall study | Total | |
|-------------------------------------------------------|---------------|-------|--|
| Number of subjects | 235 | 235 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 45.5 | | |
| standard deviation | ± 13.90 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 165 | 165 | |
| Male | 70 | 70 | |

End points

End points reporting groups

| | |
|----------------------------------------------------------------------------------------------|--------------|
| Reporting group title | Pimavanserin |
| Reporting group description: | |
| Pimavanserin 34 mg (administered as 2 x 17 mg pimavanserin tablets) once daily, for 52 weeks | |

Primary: Treatment-emergent Adverse Events (TEAEs)

| | |
|------------------------------------------------|----------------------------------------------------------|
| End point title | Treatment-emergent Adverse Events (TEAEs) ^[1] |
| End point description: | |
| Number of patients with treatment emergent AEs | |
| End point type | Primary |
| End point timeframe: | |
| 52 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 a single-arm study. Inferential testing was neither planned nor performed.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Pimavanserin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 235 | | | |
| Units: Patients | 137 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 weeks

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Pimavanserin |
|-----------------------|--------------|

Reporting group description:

Pimavanserin 34 mg (administered as 2 x 17 mg pimavanserin tablets) once daily, for 52 weeks

| Serious adverse events | Pimavanserin | | |
|---------------------------------------------------------------------|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 235 (2.13%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Diverticular perforation | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal obstruction | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal septum deviation | | | |

| | | | |
|-------------------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 235 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | | |
| occurrences causally related to treatment / all | 1 / 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 | 69 / 235 (29.36%) | | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 14 / 235 (5.96%) | | |
| occurrences (all) | 14 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 29 / 235 (12.34%) | | |
| occurrences (all) | 39 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 235 (5.11%) | | |
| occurrences (all) | 13 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 15 / 235 (6.38%) | | |
| occurrences (all) | 17 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 12 / 235 (5.11%) | | |
| occurrences (all) | 12 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 05 December 2018 | Key changes included: <ul style="list-style-type: none">- Allowed inclusion of patients beyond elderly population- Removed cognition and replaced quality of life with functional impairment and sexual functioning as exploratory assessments- Removed Mini-Mental State Examination score as exploratory safety endpoint- Removed EQ-5D as exploratory efficacy endpoint; added CSFQ-14 and KSS score as exploratory efficacy endpoints- Increased planned patient number from 290 to 420 by adding rollover patients from study ACP-103-059 in addition to -054- Revised dosing to pimavanserin 34 mg only; removed dose adjustment between 20 and 34 mg pimavanserin- Excluded patients with comorbid neurodegenerative disorders- Adapted several study procedures/timelines to align with procedures/timelines in the rollover studies 054/059- Removed rescue medication procedures |
| 18 March 2019 | <ul style="list-style-type: none">- Removed abstinence as acceptable contraception method- Implemented less restrictive definition of suicidality |
| 12 November 2019 | Key changes included: <ul style="list-style-type: none">- Added sexual dysfunction as safety endpoint- Clarified use of background antidepressants in the study- Clarified barrier methods of contraception- Clarified the assessment of heart rate for patient eligibility- Replaced BMI upper bound criterion for patient eligibility with weight increase of $\geq 7\%$ as criterion- Clarified assessment of background antidepressant adherence- Clarified follow-up procedures for discontinued patients- Tightened restrictions on controlled substances- Specified randomisation in error as major protocol deviation- Added ketamine and esketamine to the list of prohibited antidepressants and clarified timeframe for stable dosing of these drugs |
| 11 August 2020 | Key changes included: <ul style="list-style-type: none">- Added specifications for changes due to COVID-19 pandemic: visits performed remotely; use of a 6-lead ECG device at home; home delivery of study drug; study conduct, exploratory efficacy assessments, safety assessments, and unscheduled visits; COVID-19 relatedness of concomitant medications; relationship of selected AEs to COVID-19; protocol deviations related to COVID-19; remote monitoring of study sites due to travel/ visiting restrictions caused by COVID-19 pandemic; return of unused study drug and packaging when site staff visited patient's home- Allowed for interim analyses, if required for regulatory reporting |

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.

This study was terminated early by the Sponsor for business reasons due to the COVID-19 pandemic; there were no safety concerns contributing to study termination. Patients were discontinued from the study and completed safety follow-up procedures.

Notes: