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Original Research

The effects of treatment with pimavanserin on activities of daily living in patients with Parkinson's disease psychosis: a 16-week, single-arm, open-label study

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Virgilio G. H. Evidente, Daryl DeKarske, Bruce Coate and Victor Abler

Abstract

Background: More than half of patients with Parkinson's disease will experience psychosis symptoms in the form of hallucinations or delusions at some point over the course of their disease. These symptoms can significantly impact patients' health-related quality of life, cognitive abilities, and activities of daily living (ADLs) and function. Clinical assessment of how psychosis impacts these measures is crucial; however, few studies have assessed this sufficiently, in part due to a lack of appropriate scales for comprehensively assessing function.

Objective: The objective was to assess how symptoms of Parkinson's disease psychosis (PDP) impact ADLs and function, cognitive function, and health-related quality of life.

Design: To address this unmet need, we utilized a modified version of the Functional Status Questionnaire (mFSQ) to measure the impact of psychosis on ADLs and function in patients with PDP treated with pimavanserin, a US Food and Drug Administration-approved medication to treat hallucinations and delusions associated with PDP.

Methods: Eligible patients entered a 16-week, single-arm, open-label study of oral pimavanserin (34 mg) taken once daily. The primary endpoint was change from baseline to Week 16 on the mFSQ. Secondary endpoints included the Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale (MDS-UPDRS) I and II; Schwab and England ADL; Clinical Global Impression–Severity of Illness (CGI-S), Clinical Global Impression–Improvement (CGI-I), and Patient Global Impression–Improvement (PGI-I), and were also measured as change from baseline to Week 16 using mixed-effects model for repeated measures (MMRM) and least-squares mean (LSM).

Results: Our results in a proof-of-concept, 16-week, open-label clinical study in 29 patients demonstrated that an improvement in psychosis symptoms following treatment with pimavanserin was associated with improvements in multiple measures of ADLs and function. Notably, a significant improvement was found on the primary endpoint, change from baseline to Week 16 in mFSQ score [LSM [SE] 14.0 [2.50], $n = 17$; 95% CI (8.8, 19.3); $p < 0.0001$].

Conclusion: These findings highlight the potential for improvement in function with improvement of psychosis symptoms in patients with PDP and suggest that the mFSQ may be a measurement tool to evaluate the level of improvement in function.

Trial registration: ClinicalTrials.gov Identifier: NCT04292223.

Keywords: neurodegenerative disorders, Parkinson's disease, pimavanserin, psychosis, safety, tolerability

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Correspondence to:
Virgilio G. H. Evidente
Movement Disorders Center of Arizona, 9500 E. Ironwood Square Drive, Suite 118, Scottsdale, AZ 85258, USA
vevidente@movementdisorders.us

Daryl DeKarske
Bruce Coate
Victor Abler
Acadia Pharmaceuticals Inc., San Diego, CA, USA

Introduction

More than half of patients with Parkinson's disease (PD) will develop psychosis at some point over the course of their disease.[1,2] Parkinson's disease psychosis (PDP) presents as hallucinations or delusions[2] and is observed in 45–68% of patients.[3] PDP is associated with a decreased quality of life, increased nursing home placement and mortality, and behavioral and sleep disturbances.[4–6] Importantly, PDP can also cause functional limitations as a result of worsening psychosis, placing a greater burden on patients and their caregivers.[6,7] Patients with PDP often understate their level of disability[8] and tend to have poor insight regarding the impact of PDP on their daily function,[8] which further increases caregiver burden[6] and, in many cases, leads to psychological burden,[9] depressed mood,[9] and reduced quality of life.[10] Objective assessments of daily functioning in patients with PDP are therefore essential to better understand the impact of treatment on both psychosis and function. However, prior studies of activities of daily living (ADLs) have used the Unified Parkinson's Disease Rating Scale (UPDRS),[11] which is more focused on motor function and thus does not provide adequate insight into the impact of psychosis on function.[8,12] Additionally, although many scales exist for assessing psychosis symptoms, each has specific strengths and limitations,[13] and there is no scale that is considered the standard for measuring daily functioning in patients with PDP.[12]

Pimavanserin is a selective 5-hydroxytryptamine receptor 2A (5-HT_{2A}) inverse agonist and antagonist, with some additional selectivity for the 5-HT_{2C} receptor, that was approved by the US Food and Drug Administration in 2016 to treat hallucinations and delusions associated with PDP.[11,14,15] Pimavanserin, *in vitro*, has shown no meaningful binding affinity to any other G protein-coupled receptor,[14,16] including dopaminergic, muscarinic, histaminergic, and adrenergic receptors, which may be associated with off-target effects from other atypical antipsychotic drugs.

This 16-week, open-label study is the first to utilize several validated assessment tools to evaluate the effects of pimavanserin on ADLs and function and psychosis symptoms in patients with PDP. We utilized a modified version of the Functional Status Questionnaire (mFSQ) to help measure changes in ADLs and function associated with a reduction in symptoms of psychosis in patients with PDP.

Methods

Eligibility

Eligibility criteria for the study included (1) diagnosis of PD with psychosis symptoms that may impair function and are severe enough to warrant treatment with an antipsychotic agent; (2) a Clinical Global Impression–Severity of Illness (CGI-S) score ⩾4 at screening and baseline, a Schwab and England ADL scale score of 40–80% (inclusive) at screening and baseline, and a Mini-Mental State Examination (MMSE) score ⩾19 at screening; (3) ability to designate a caregiver or study partner who could provide reliable information regarding the patient's well-being and written informed consent and attend all clinic visits; (4) if on anti-Parkinsonian medication, must be on a stable regimen ⩾2 months prior to baseline; and (5) provided written informed consent. Criteria for the diagnosis of PD psychosis were the presence of hallucinations and/or delusions in a patient with a clinical diagnosis of idiopathic PD according to the Movement Disorders Society criteria for the diagnosis of PD. PD psychosis was diagnosed largely by a neurologist or movement specialist treating patients' PD symptoms.

Study design

Between 10 February 2020 and 26 April 2022, patients with PDP entered a 16-week, multicenter, single-arm, open-label study (NCT04292223) to evaluate the effects of pimavanserin on the mFSQ [Figure 1(a)]. A total of 70 patients were screened, and 29 patients were enrolled in the study. All eligible patients received open-label pimavanserin 34 mg taken orally once daily. The study included three periods: screening (3–35 days), treatment (16 weeks), and safety follow-up [30–34 days; Figure 1(b)]. The study was conducted on an outpatient basis, with visits at screening; baseline (Week 0); Weeks 2, 4, 8, 12, and 16; and a follow-up visit (30–34 days after the last dose of pimavanserin). All study visits occurred at clinics within the United States.

This study utilized several scales to measure ADLs and function, with some scales assessed by both patient and caregiver. The scales included (1) a mFSQ, which was modified to exclude the

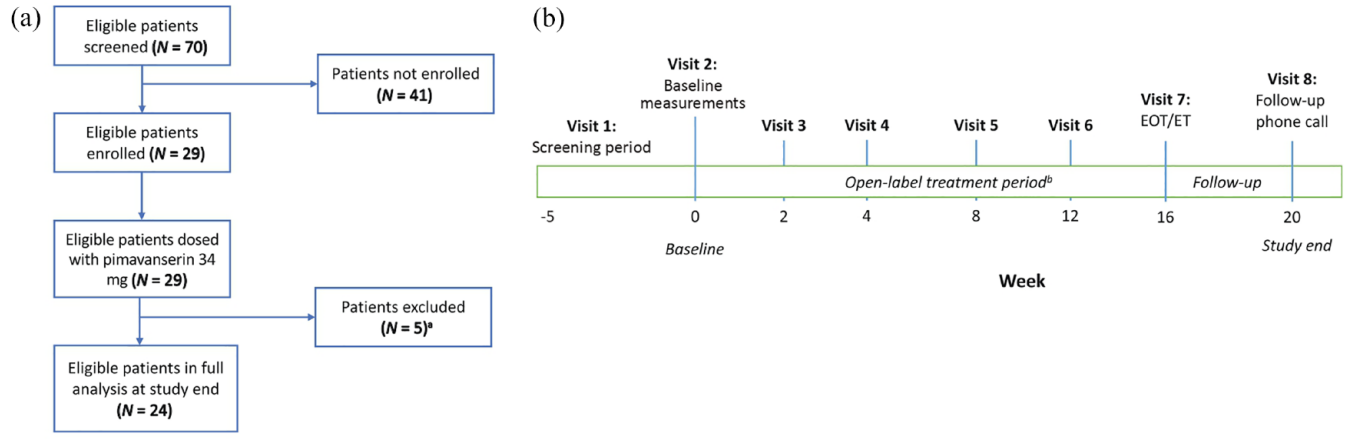

Figure 1. Study design: (a) patient flowchart and (b) experimental timeline.
[a]Patients were excluded from studies because of noncompliance with the study drug ($n = 2$; 6.8%), any treatment-emergent adverse event [electrocardiogram QT prolonged ($n = 1$; 3.4%), relocation out of state ($n = 1$; 3.4%), and loss to follow-up ($n = 1$; 3.4%)].
[b]Open-label treatment period included assessment of primary and secondary endpoints: Schwab and England ADL scale score; Clinical Global Impression–Improvement scale score; Clinical Global Impression–Severity scale score; Movement Disorders Society–Unified Parkinson's Disease Rating Scale score; Patient Global Impression–Improvement scale score.
EOT/ET, end of trial/early termination.

work performance subscale owing to the age and nonemployment status of the PDP population; (2) the Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I (nonmotor aspects of the experience of daily living) and Part II (motor aspects of the experience of daily living); (3) the Schwab and England Patient and Caregiver scale (to ensure inclusion of patients with sufficient disability); (4) the Patient Global Impression–Improvement (PGI-I) scale; (5) the Clinical Global Impression–Improvement (CGI-I) scale; and (6) the CGI-S scale. A follow-up safety assessment telephone call was conducted at least 30 days but not more than 34 days after the last dose of the study drug. Acadia obtains licenses for use of all scales in all of its clinical trials.

Assessments

The primary endpoint of the study was the change from baseline to Week 16 on a mFSQ, a brief, standardized, self-administered questionnaire that provides a comprehensive assessment of physical, psychological, and social functions.[17] This scale was chosen for this study because its use has been recommended by the International Parkinson and Movement Disorder Society. The scale was modified to have the work performance subscale removed for use in this study since most of the patients included were elderly and not employed, and thus, it was not applicable for this patient population. Details of the mFSQ and the questions used in the study are reported in Supplemental Table 1. The secondary endpoints [MDS-UPDRS I and II (caregiver and patient versions); Schwab and England ADL scale (caregiver and patient versions); CGI-S (clinician rated); CGI-I (clinician rated); and PGI-I (patient rated)], a series of validated tools used to assess patients' global function, including severity and improvement in hallucination/delusions,[12,18–20] were also measured as the change from baseline to Week 16. The CGI-S, CGI-I, and PGI-I were focused on psychosis symptoms.

Exploratory endpoints assessed the demand placed on caregivers and families due to PDP, measured as change from baseline to Week 16. These included the Caregiver Strain Index (CSI) total score and the patient-rated Neuropsychiatric Inventory–Questionnaire (NPI-Q; Nighttime Behavior Domain Severity and Caregiver Distress). Additional exploratory endpoints assessed the effects of pimavanserin on depressive symptoms [Geriatric Depression Scale (GDS); patient-rated], cognition (mFSQ score, by subscale), and functional capacity [Virtual Reality

Functional Capacity Assessment Tool (VRFCAT)], all measured as the change from baseline to Week 16.

Safety and tolerability were assessed through clinical evaluations, including physical examinations and electrocardiograms, regularly throughout the study to identify treatment-emergent adverse events (TEAEs). Laboratory evaluations were conducted at screening (Visit 1), baseline (Visit 2), as well as at Visits 4, 5, 6, and 7 (at which end of treatment occurred). Suicidality was assessed throughout the study using the Columbia-Suicide Severity Rating Scale (C-SSRS).

Statistical analysis

All safety and efficacy measures were summarized using descriptive statistics. Mixed-effects models for repeated measures (MMRM) and least-squares means (LSMs) were used to analyze continuous outcome measures for primary and secondary outcomes. For each continuous outcome (except for CGI-I and PGI-I), the dependent variable was the change from baseline values, and the independent variables in the model included effects for visit, baseline value, and baseline value-by-visit interaction. An unstructured covariance matrix was used to model the within-subject errors, and the Kenward-Roger approximation was used to adjust the denominator degrees of freedom. For CGI-I, the dependent variable was the CGI-I score, and the independent variables in the model included effects for visit, baseline CGI-S score, and baseline CGI-S score-by-visit interaction. For PGI-I, the dependent variable was the PGI-I score, and the independent variable in the model was visit.

Summary statistics, including the LSM and 95% CI by visit, are reported. This was an exploratory study and thus was not powered to detect statistical significance. Formal sample size calculations were not used to determine sample size. The full analysis set included subjects who received at least one dose and had both a baseline and at least one postbaseline value for the mFSQ score. The safety analysis set included data from subjects who received at least one dose of pimavanserin. Adverse events were defined as those occurring after the first dose and up to 30 days after the last dose of the study drug.

Results

Patient disposition and baseline characteristics

Seventy patients with PDP were screened; of those, 29 patients entered the study and were treated with pimavanserin, and 24 (82.8%) patients completed the study [Figure 1(a)]. At baseline, patients were of a mean age of 70.2 years; 62.1% were male, 96.6% were White, 96.6% were living at home, and 51.7% had a spouse or partner as their caregiver (Table 1). The mean (SE) score for MMSE was 24.9 (0.43), mFSQ was 61.5 (2.97), MDS-UPDRS Part I was 18.3 (0.92), MDS-UPDRS Part II was 17.4 (1.41), CGI-S was 4.1 (0.05), patient-reported Schwab and England ADL scale was 65.4 (2.74), and caregiver-reported Schwab and England ADL scale was 62.5 (2.85) (Table 1). These scores indicated that the patients enrolled in this study were truly disabled. None of the patients reported suicidal ideation or behavior, as rated by the C-SSRS, at baseline or screening (Table 1). Out of the 29 patients, 5 terminated the study early: 2 due to noncompliance with the study drug, 1 for TEAEs, 1 for relocation out of state, and 1 due to loss to follow-up [Figure 1(a); Table 2].

ADLs and function assessments

Patients demonstrated significant improvements in LSM [standard error (SE)] mFSQ score change from baseline to Week 16 [14.0 [2.50], $n=17$; 95% CI (8.8, 19.3); $p<0.0001$] (Figure 2), which was the primary endpoint. Changes in the mFSQ were seen as early as Week 12 ($p<0.0001$). When analyzed by subscale, improvements were also seen at Week 16 on the Physical Function: Basic ADL subscale [8.1 [2.41], $n=22$; 95% CI (3.1, 13.1); $p=0.0031$], the Physical Function: Intermediate ADL subscale [7.0 [3.00], $n=21$; 95% CI (0.8, 13.3); $p=0.0286$], the Psychological Function: Mental Health subscale [13.3 [1.94], $n=22$; 95% CI (9.3, 17.4); $p<0.0001$], the Social Activity subscale [25.8 [7.52], $n=18$; 95% CI (10.2, 41.5); $p=0.0026$], and the Quality of Interaction subscale [12.3 [2.07], $n=22$; 95% CI (8.0, 16.6); $p<0.0001$]. Improvements were seen as early as Week 12 in the Physical Function: Intermediate ADL subscale ($p=0.0174$) and the Social Activity subscale ($p=0.0074$), Week 4 in the Psychological Function: Mental Health subscale ($p=0.0079$),

Table 1. Baseline demographics and disease characteristics.

Characteristics	Pimavanserin 34 mg, *N* = 29
Age, mean (range)	70.2 (41–87)
Male, *n* (%)	18 (62.1)
Race, *n* (%)	
White	28 (96.6)
Black/African American	1 (3.4)
Ethnicity, *n* (%)	
Hispanic or Latino	7 (24.1)
Not Hispanic or Latino	22 (75.9)
Living situation, *n* (%)	
At home	28 (96.6)
In a facility	1 (3.4)
Caregiver relationship, *n* (%)	
Spouse/partner	15 (51.7)
Child	4 (13.8)
Other family member	1 (3.4)
Friend	8 (27.6)
Other	1 (3.4)
Suicidal ideation at baseline, C-SSRS	
Yes, *n* (%)	0 (0.0)
No, *n* (%)	29 (100%)
MMSE total score, mean (SE)	24.9 (0.43)
mFSQ score, mean (SE)	61.5 (2.97)
MDS-UPDRS Part I (nonmotor ADL), mean (SE)	18.3 (0.92)
MDS-UPDRS Part II (motor ADL), mean (SE)	17.4 (1.41)
CGI-S score, mean (SE)	4.1 (0.05)
GDS score, mean (SE)	4.5 (0.5)
Schwab and England score (patient), mean (SE)[a]	65.4 (2.74)
Schwab and England score (caregiver), mean (SE)[a]	62.5 (2.85)
Baseline NPI delusions total score, mean (SE)	4.3 (0.59)
Baseline NPI hallucinations total score, mean (SE)	5.6 (0.44)

[a]N = 28.
ADL, activity of daily living; CGI-S, Clinical Global Impression–Severity of Illness; C-SSRS, Columbia-Suicide Severity Rating Scale; GDS, Geriatric Depression Scale, MDS-UPDRS, Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale; mFSQ, modified Functional Status Questionnaire; MMSE, Mini-Mental Status Examination; NPI, Neuropsychiatric Inventory; PGI, Patient Global Impression–Improvement.

Table 2. Summary of TEAEs.

Characteristics	Pimavanserin 34 mg, *N* = 29	
	Patients, *n* (%)	Events
Any TEAE	11 (37.9)	27
Any serious TEAE[a]	3 (10.3)	3
Any related TEAE	–	–
Any related serious TEAE	–	–
Any TEAE leading to study-drug discontinuation[b]	1 (3.4)	1
Any severe TEAE[c]	1 (3.4)	1
Any fatal TEAE	–	–

[a]Hyperuricemia (*n* = 1; 3.4%); syncope (*n* = 1; 3.4%); hypotension (*n* = 1; 3.4%).
[b]Electrocardiogram QT prolonged (*n* = 1; 3.4%).
[c]Squamous cell carcinoma (*n* = 1; 3.4%).
TEAE, treatment-emergent adverse event.

and Week 8 in the Quality of Interaction subscale ($p = 0.0007$).

Significant improvements from baseline to Week 16 were also observed across CGI-S [−1.5 [0.25], $n = 22$; 95% CI (−2.0, −1.0); $p < 0.0001$] and CGI-I scores [1.9 [0.17], $n = 22$; 95% CI (1.6, 2.3); $p < 0.0001$] [Figure 3(a)]. Significant improvements on both of these scales were seen as early as Week 2 (CGI-S: $p = 0.0081$; CGI-I: $p = 0.0004$).

Scores on MDS-UPDRS Part I [−6.3 [0.97], $n = 22$; 95% CI (−8.3, −4.3); $p < 0.0001$] and MDS-UPDRS Part II [−2.6 [0.98], $n = 22$; 95% CI (−4.6, −0.5); $p = 0.0165$] [Figure 3(b)] improved significantly from baseline to Week 16. Significant improvement was also observed in the PGI-I score from baseline to Week 16 [2.0 [0.22], $n = 22$; 95% CI (1.6, 2.5); $p < 0.0001$] [Figure 3(c)]. Additionally, on the PGI-I and MDS-UPDRS Part I scales, scores significantly improved as early as Week 2 (all $p < 0.05$). Numeric improvement was observed in the Schwab and England ADL score, although it did not reach statistical significance [3.4 [2.97], $n = 22$; 95% CI (−2.7, 9.5); $p > 0.05$] (Figure 4).

Exploratory endpoints

A significant change was seen from baseline to Week 16 in CSI total score [−1.6 [0.35], $n = 22$; 95% CI (−2.3, −0.9); $p < 0.001$] (Supplemental Figure 1); significant improvements were seen beginning at Week 4 ($p = 0.0049$). Additionally, significant improvements were seen in both sleep severity [−0.9 [0.17], $n = 22$; 95% CI (−1.2, −0.5); $p < 0.0001$] (Supplemental Figure 2A) and sleep distress [−0.9 [0.27], $n = 12$; 95% CI (−1.5, −0.3); $p < 0.01$] (Supplemental Figure 2B)

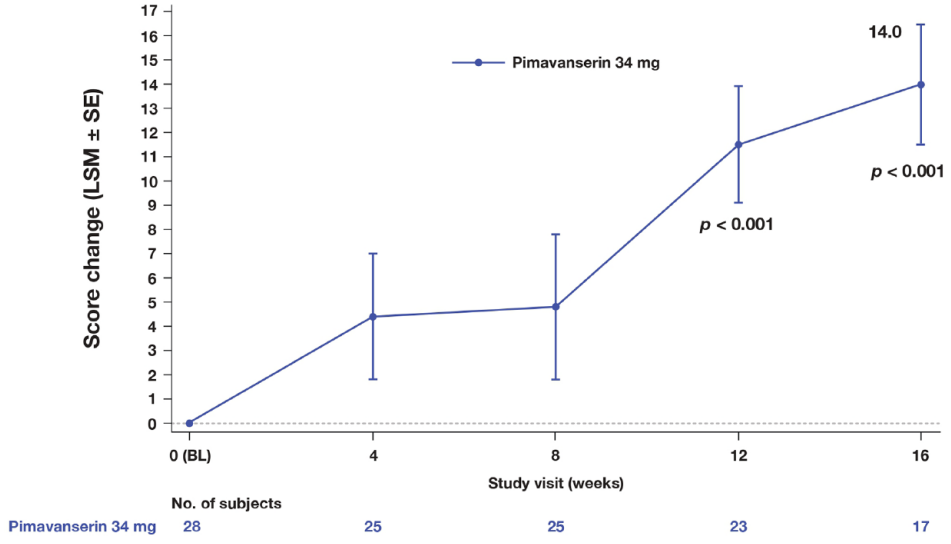

Figure 2. mFSQ score change from baseline by visit.
*Scale is standardized from 0 to 100; the baseline score was 61.5.
BL, baseline; LSM, least-squares mean; mFSQ, modified Functional Status Questionnaire; SE, standard error.

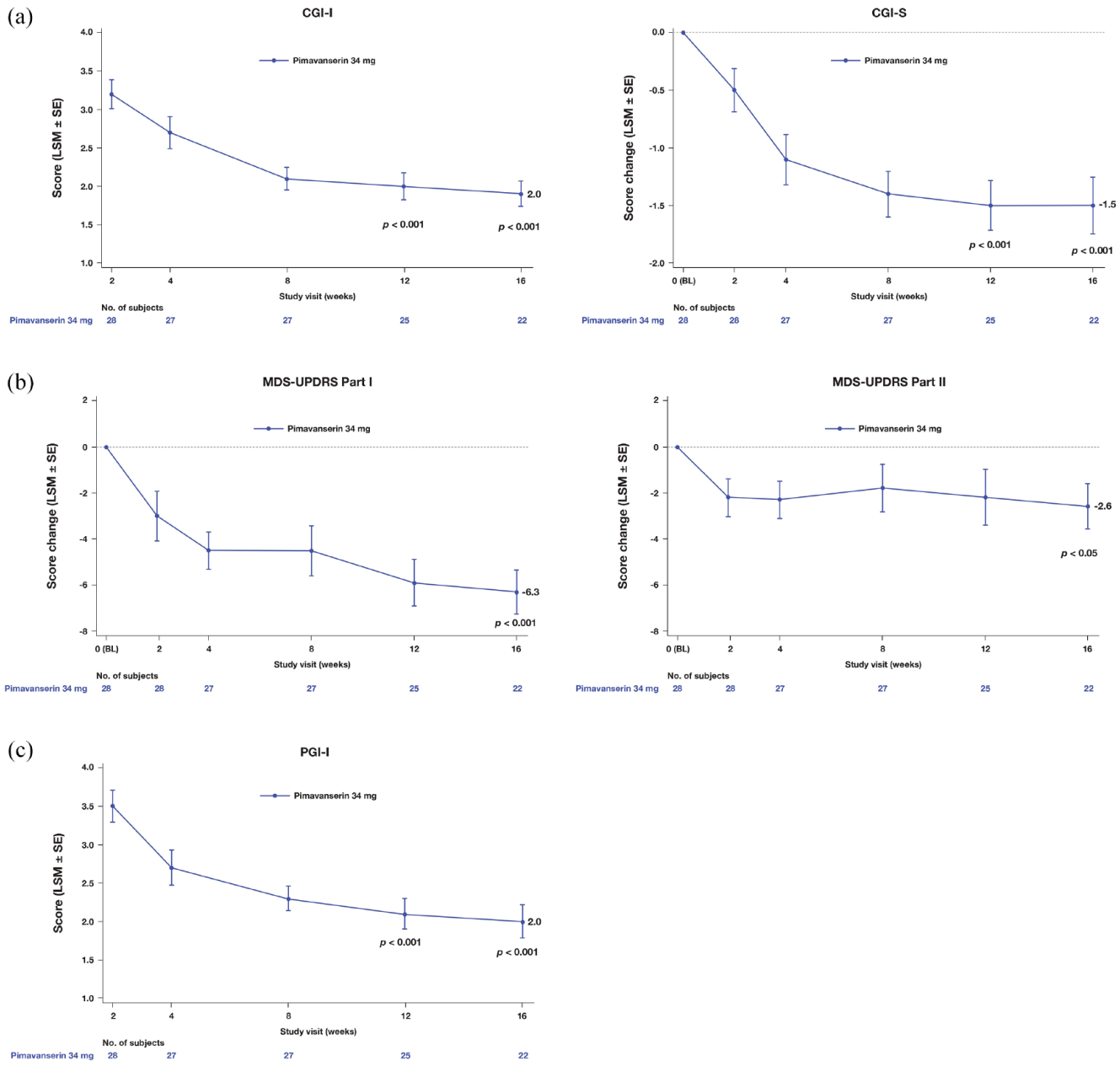

Figure 3. (a) CGI-I and CGI-S score changes from baseline by visit; (b) MDS-UPDRS Part I (nonmotor ADL) and II (motor ADL) total score by visit; (c) PGI-I scores by visit.
ADL, activity of daily living; BL, baseline; CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impression–Severity; LSM, least-squares mean; MDS-UPDRS, Movement Disorders Society–Unified Parkinson's Disease Rating Scale; PGI-I, Patient Global Impression–Improvement; SE, standard error.

scores on the NPI-Q at Week 16. Improvement was consistently seen starting at Week 2 in sleep severity ($p=0.0017$) and Week 4 in sleep distress ($p=0.0131$) scales. Scores on the GDS also significantly improved at Week 16 [−1.0 [0.33], $n=22$; 95% CI (−1.7, −0.3); $p<0.01$] (Supplemental Figure 3); improvements were seen as early as Week 12 ($p=0.0036$). No changes were observed in total error count [0.8 [0.86], $n=19$; 95% CI (−1.0, 2.6); $p>0.05$] (Supplemental Figure 4A) or total time to complete in seconds [−57.1 [64.06], $n=19$; 95% CI (−192.1, 77.8); $p>0.05$] (Supplemental Figure 4B) in the VRFCAT at Week 16.

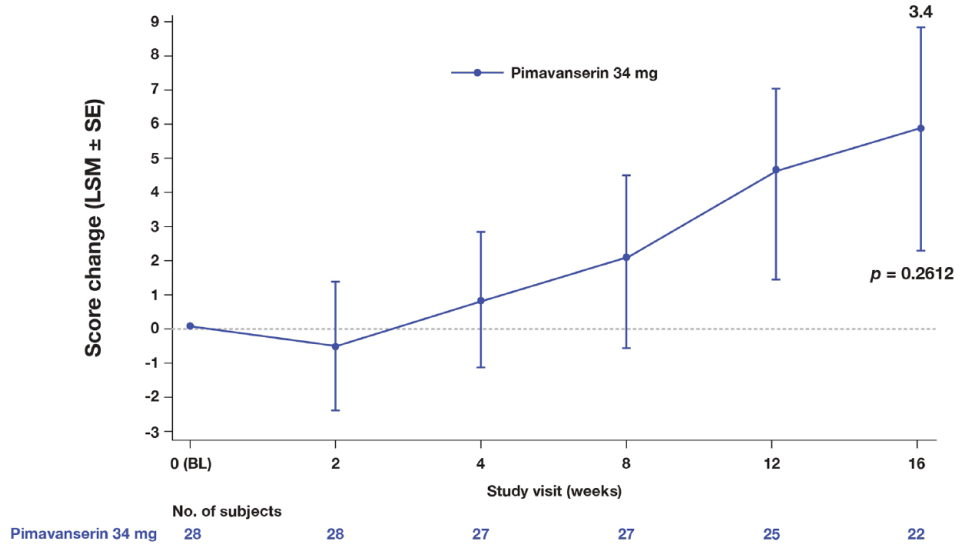

Figure 4. Schwab and England ADL patient score change from baseline to Week 16.
ADL, activity of daily living; BL, baseline; LSM, least-squares mean; SE, standard error.

Safety and tolerability

In total, 27 TEAEs ($n = 11$) were reported throughout the study period. There were 3 (10.3%) serious TEAEs: hyperuricemia ($n = 1$; 3.4%), syncope ($n = 1$; 3.4%), and hypotension ($n = 1$; 3.4%). There was also 1 (3.4%) severe TEAE (squamous cell carcinoma) and 1 TEAE leading to study-drug discontinuation (electrocardiogram QT prolonged). These TEAEs were consistent with the established safety profile of pimavanserin seen in the clinical studies, and no new safety signals were observed during the study.

Discussion

Results of this 16-week, open-label study revealed a significant improvement overall in ADL and functional outcomes, as measured by the mFSQ in patients with PDP following treatment with pimavanserin.

Additionally, pimavanserin significantly reduced CGI-I and CGI-S scores, indicating an improvement in the severity of psychosis symptoms and functioning compared with baseline (CGI-I) and compared with other patients with PDP (CGI-S). Similarly, patients rated an improvement in their own symptoms following treatment, as indicated by reduced scores on PGI-I. These findings demonstrate a parallel improvement in psychosis symptom scores with an improvement in functional outcome scores.

Scores on the MDS-UPDRS Parts I and II were also reduced following pimavanserin treatment, showing improvement in both motor- and non-motor-related ADLs and function. Additionally, beneficial effects of treatment with pimavanserin were seen on exploratory measures of caregiver strain, quality of sleep, and depression scores. Importantly, patients showed improvement in many of these measures earlier in treatment, and this improvement persisted throughout the treatment course. Overall, these results suggest that improvement in psychosis is also accompanied by an improvement in ADLs and function, based on both patient- and caregiver-related scores.

Although scores on the Schwab and England ADL scale numerically improved, they did not reach statistical significance; however, this tool was used to screen for the inclusion of patients with sufficient disability rather than as a tool for measuring the efficacy of interventions. Although no significant effects were seen in functional capacity on the VRFCAT, it is possible that due to the virtual reality format, in addition to possible challenges related to manual dexterity, this task may not have provided a favorable metric for evaluating functionality in this study.

Patients do not always have good insight into their own condition or symptoms[8]; thus, using caregiver reports in addition to patient reports provides useful information regarding the efficacy

of pimavanserin on psychosis symptom severity. Additionally, the impact of patients' conditions on caregiver burden, burnout, and quality of life is relevant for understanding the impact of the disease on caregivers[6,10,21,22] and can be informative for understanding health-related costs[23] owing to increased nursing home placement[21] and other inpatient and outpatient health resource utilization.[23] The mFSQ and the other assessments evaluated in this study are crucial for improving our understanding of the overall impact of treatments for psychosis symptoms of PDP on patient function, not just the impact of these treatments on disease-specific metrics.

The assessment of ADLs and function of patients with PDP can be used to better inform treatment effects. In this study, we aimed to represent the wide range of causes of ADL deficits; the mFSQ in particular provides information on several domains of patient health and health-related quality of life (including physical, psychological, and social role functions and social activity domains), allowing for a comprehensive assessment of the impact of treatment with pimavanserin on ADLs and function in patients with PDP. Mental health and social interaction deficits can contribute to overall disability in this patient population and prevent patients from completing daily tasks and other ADLs; thus, accurate assessment of different contributions to disability is important given that the onset of functional limitations triggers changes in clinical management, including adjustment of medications or referral for deep-brain stimulation surgery. Future controlled studies assessing efficacy for improvement of psychosis symptoms and impact on ADLs and function should consider taking this approach.

Limitations of the study include the small patient size and its design (open-label). An additional limitation is that this study occurred during the COVID-19 pandemic; restrictions and difficulties surrounding recruiting and retaining patients during the pandemic contributed to the small sample size and large screening failure rate (41/70). In addition, patient difficulty reporting outcome measures using a handheld device, and exclusion due to MMSE scores or the presence of another condition such as dementia, contributed to the screening failure rate. It also was not powered to detect statistical significance. Although this single-arm study suggests an impact on functioning in PDP patients treated with pimavanserin, these results are preliminary in nature. Therefore, while results from the current study suggest that the efficacy of pimavanserin in improving psychosis symptoms is associated with improved ADL and function in patients with PDP, larger and longer-term controlled studies, including those comparing pimavanserin to other antipsychotics or placebo, are needed to confirm these findings.

Conclusion

Our findings in this 16-week open-label study indicate that pimavanserin treatment for the improvement of hallucinations and delusions in patients with PDP is associated with an improvement in ADLs and function. In addition to the improvements in mFSQ score, the significant improvements in CGI-I and PGI-I scores highlight both a clinical and patient perception of improved psychosis symptoms. Taken together, these findings suggest that treatment with pimavanserin can result in both an improvement in psychosis and corresponding improvements in various health outcomes and health-related quality of life metrics, including physical and psychological functions, as well as typical ADLs required for day-to-day activities such as eating, dressing, and bathing. Additionally, results from this study highlight both the importance of evaluating and the clinical relevance of the impact of treatment on ADLs and function for patient outcomes. These data support the potential for further clinical research assessing ADLs and function in patients with PDP utilizing the mFSQ in longer-term and larger controlled studies.

Declarations

Ethics approval and consent to participate

This study was approved by the IRB (20192825) and performed in compliance with the Declaration of Helsinki and is consistent with International Council for Harmonisation/Good Clinical Practice and applicable regulatory requirements. Written informed consent was required for eligibility to participate in this study.

Consent for publication

Not applicable.

Author contributions

Virgilio G. H. Evidente: Investigation; Writing – review & editing.

Daryl Dekarske: Methodology; Validation; Writing – review & editing.

Bruce Coate: Data curation; Formal analysis; Methodology; Writing – review & editing.

Victor Abler: Conceptualization; Funding acquisition; Methodology; Project administration; Writing – review & editing.

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Competing interests

VGHE has received personal compensation for serving as a consultant or speaker for Adamas, Amneal, Kyowa Kirin, Ipsen, Lundbeck, Medtronic, Merz, Neurocrine, Revance, Sunovion, Teva, and UCB; and has received research support from AbbVie, Acadia, Aeon, Aptinyx, CND Life Sciences, Ipsen, IRLAB, Jazz Pharmaceuticals, Lundbeck, Neuraly, Neurocrine, Pharma Two B, Revance, Scion Neurostim, and Sunovion. DD, BC, and VA are employees of Acadia Pharmaceuticals Inc.

Availability of data and materials

Clinical study documents are confidential and the property of Acadia. The protocol or statistical analysis plan is available upon request.

Supplemental material

Supplemental material for this article is available online.

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