A 16-Week Open-Label Study of the Effects of Treatment With Pimavanserin on Activities of Daily Living in Subjects With Parkinson's Disease Psychosis (PDP)

Virgilio G. H. Evidente,[1] Daryl DeKarske,[2] Bruce Coate,[2] Victor Abler*[2]

[1]Movement Disorders Center of Arizona, Scottsdale, AZ, USA; [2]Acadia Pharmaceuticals Inc., San Diego, CA, USA

*Presenting author

INTRODUCTION

- An accurate assessment of disabilities associated with Parkinson's Disease Psychosis (PDP) is essential because functional limitations can result from a worsening of psychosis
- Unfortunately, there is a paucity of studies evaluating this risk with validated clinical assessment tools
- Patient insight into their daily functioning abilities also varies, as patients with PD tend to understate their level of disability[1]
  - Therefore, it is important to integrate data from multiple sources (examination, disability assessment, and patient and caregiver reports) to assess patient disability
- The Functional Status Questionnaire (FSQ) is a brief, standardized, self-administered questionnaire that provides a comprehensive assessment of physical, psychological, social, and role functions in patients[2]
- The Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale (MDS-UPDRS), the Schwab and England Patient and Caregiver Scale, the Patient Global Impression of Improvement (PGI-I) Scale, and the Clinical Global Impression–Improvement (CGI-I) and –Severity of Illness (CGI-S) Scales are additional validated tools that can be used to assess a patient's global function[3-6]
- This open-label, 16-week, phase 4 study (NCT04292223) in PDP patients was the first to evaluate the impact of pimavanserin on activities of daily living (ADL) in patients using a modified version of the FSQ (mFSQ) and other scales that measure function as assessed by both the patient and caregiver

METHODS

- Eligible patients were adults ≥40 years of age with a diagnosis of PDP, psychosis symptoms severe enough to warrant treatment with an antipsychotic agent, a CGI-S score ≥4, a Schwab & England ADL Scale score of 40%-80% (inclusive), and a Mini-Mental State Examination (MMSE) score ≥19 at screening and baseline
- After screening, patients entered a 16-week, single-arm, open-label study of once-daily oral pimavanserin 34 mg (**Figure 1**)
- The primary endpoint was the time change from baseline on the Modified Functional Status Questionnaire score (excludes the work performance subscale) at Week 16
- Secondary endpoints (MDS-UPDRS Parts I & II, Schwab and England ADL, and CGI-S) were measured as changes from baseline to Week 16 or scores at Week 16 (CGI-I and PGI-I)
- Safety was measured based on treatment-emergent adverse events (TEAEs) and potentially clinically important findings from clinical and laboratory assessments
- Statistical methods to analyze continuous outcomes included the mixed-effects model for repeated measures (MMRM) and least-squares means (LSM)

RESULTS

- A total of 29 patients were treated with pimavanserin 34 mg once daily, of whom 24 (82.8%) completed the study; 5 patients terminated the study early: 2 due to noncompliance with the study drug and 1 each for TEAEs, other (relocation out of state), and loss to follow-up
- Patients were a mean of 70.2 years of age, 62.1% were male, and 96.6% were living at home at baseline (**Table 1**)
- Patients treated with pimavanserin demonstrated significant improvements in LSM (standard error [SE]) mFSQ score change from baseline to week 16 (14.0 [2.50]; $p < 0.05$) (**Figure 2**)
- There were significant improvements from baseline to week 16 in the CGI-S scores (-1.5 [0.25]) (**Figure 3a**) and CGI-I scores (1.9 [0.17]) (**Figure 3b**) in patients treated with pimavanserin (nominal $p < 0.05$ for both)
- Scores on MDS-UPDRS Part I (-6.3 [0.97]) (**Figure 4a**) and MDS-UPDRS Part II (-2.6 [0.98]) (**Figure 4b**) improved significantly from baseline to week 16 in patients treated with pimavanserin (nominal $p < 0.05$)
- Among patients treated with pimavanserin, there were significant ($p < 0.05$) improvements from baseline to Week 16 in PGI-I scores (2.0 [0.22]) (**Figure 5**)
- There were 3 (10.3%) serious TEAEs, 1 (3.4%) severe TEAE, and 1 (3.4%) TEAE leading to study-drug discontinuation (**Table 2**)
- Pimavanserin was well-tolerated, and there were no new safety signals observed during the study

REFERENCES

1. Shulman LM, et al. *Mov Disord* 2006;21(6):794-9.
2. Jette AM, et al. *J Gen Intern Med* 1990;(1):143-9.
3. Rodriguez-Blazquez C, et al. *Parkinsonism Relat Disord* 2013;19(10):889-93.
4. McRae C, et al. *Mov Disord* 2000;15(2):335-6.
5. Busner J, Targum SD. *Psychiatry (Edgmont)* 2007;4(7):28-37.
6. Bouca-Machado R, et al. *Front Neurosci* 2022;16:945398.

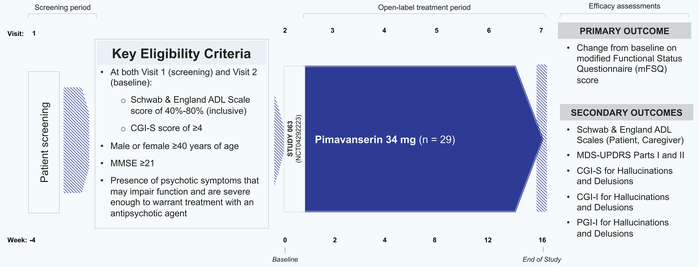
ACKNOWLEDGMENTS

Medical writing support was provided by CITRUS Health Group (United States), which was in accordance with Good Publication Practice (GPP3) guidelines and funded by Acadia Pharmaceuticals Inc. (San Diego, CA, USA).

DISCLOSURES

This study was funded by Acadia Pharmaceuticals Inc. (San Diego, CA, USA). V.G.H.E. has received personal compensation for serving as a consultant or speaker for Adamas, Amneal, Bayvanza, Teva, Kyowa Kirin, Lundbeck, UCB, Teva, Ipsen, Merz, Medtronic, Neurocrine, and Sunovion. V.G.H.E. has received research support from AbbVie, Acadia, Axon, Aptinyx, Lundbeck, Neuraly, Pharma Two B, Bevance, and Sunovion. DD, BC, and VA are employees of Acadia Pharmaceuticals Inc.

Figure 1. Study design



ADL, activities of daily living; CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impression–Severity of Illness; MDS-UPDRS, Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale; MMSE, Mini-Mental Status Examination; PGI-I, Patient Global Impression of Improvement.

Table 1. Baseline demographics and disease characteristics

Characteristic	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)
MMSE total score, mean (SD)	24.9 (2.31)
mFSQ score, mean (SD)	61.5 (15.70)
MDS-UPDRS Part I (Nonmotor ADL), mean (SD)	18.3 (4.97)
MDS-UPDRS Part II (Motor ADL), mean (SD)	17.4 (7.61)
CGI-S score, mean (SD)	4.1 (0.26)
CGI-I score, mean (SD)	1.9 (0.17)
PGI-I score, mean (SD)	2.0 (0.22)
Schwab and England score (patient), mean (SD)	65.4 (2.74)
Schwab and England score (caregiver), mean (SD)	62.5 (2.85)

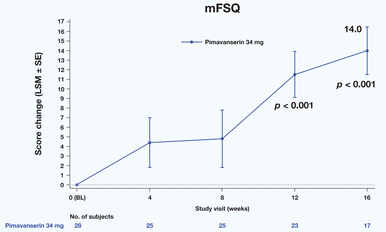
CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impression–Severity of Illness; MDS-UPDRS, Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale; mFSQ, Modified Functional Status Questionnaire; MMSE, Mini-Mental Status Examination; PGI, Patient Global Impression–Improvement; SD, standard deviation.

Table 2. Summary of TEAEs

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

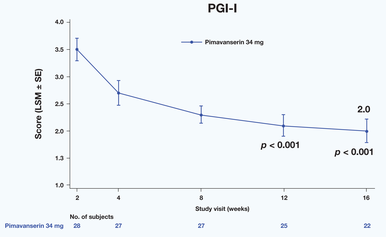
TEAE, treatment-emergent adverse event.

Figure 2. Modified Function Status Questionnaire (mFSQ) score change from baseline by visit



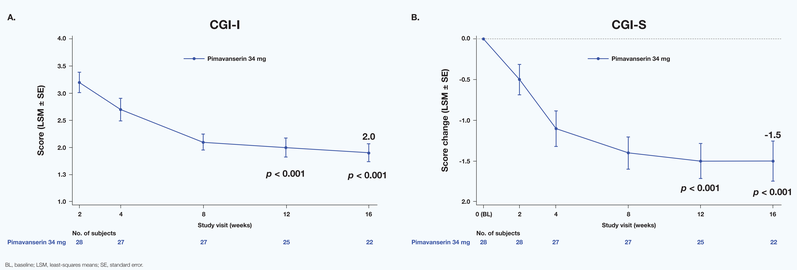
*Scale is standardized from 0-100; the baseline score was 61.5.
BL, baseline; LSM, least-squares means; SE, standard error.

Figure 5. Patient Global Impression of Improvement (PGI-I) scores by visit



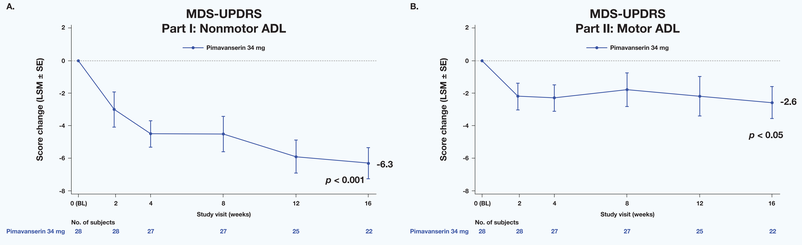
LSM, least-squared means; SE, standard error.

Figure 3. (A) Clinical Global Impressions–Improvement (CGI-I) and (B) Clinical Global Impressions–Severity (CGI-S) score changes from baseline by visit



BL, baseline; LSM, least-squares means; SE, standard error.

Figure 4. Movement Disorder Society–Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score by visit: (A) Part I, Nonmotor ADL and (B) Part II, Motor ADL



ADL, activities of daily living; BL, baseline; LSM, least-squares means; SE, standard error.

CONCLUSIONS

- Functional outcomes and psychosis measures improved with pimavanserin 34 mg once-daily treatment over 16 weeks
- All primary and secondary measures showed a statistically significant change from baseline to endpoint, except the Schwab and England scale
- There were no new safety findings in the study
- These data support the potential for new research that further assesses activities of daily living and other functional improvements in patients with psychosis

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