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)

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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]; $p < 0.0001$) (**Figure 2**)
- There were significant improvements from baseline to week 16 in the CGI-S scores (-1.5 [0.22]) (**Figure 3a**) and CGI-I scores (1.9 [0.17]) (**Figure 3b**) in patients treated with pimavanserin (nominal $p < 0.0001$ for both)
- Scores on MDS-UPDRS Part I (-6.3 [0.97]; $p < 0.0001$) (**Figure 4a**) and MDS-UPDRS Part II (-2.6 [0.98]; $p < 0.017$) (**Figure 4b**) improved significantly from baseline to week 16 in patients treated with pimavanserin
- Among patients treated with pimavanserin, there were significant ($p < 0.0001$) 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

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DISCLOSURES
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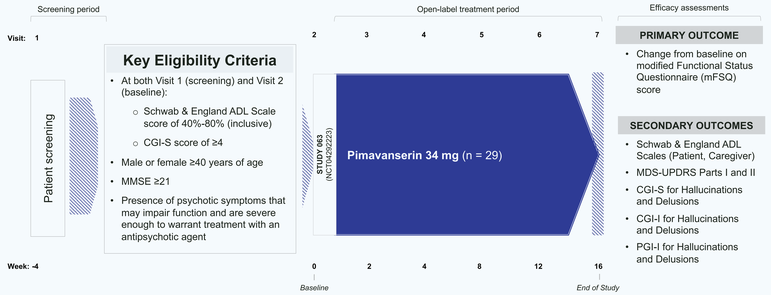
Figure 1. Study design



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 (SE)	24.9 (0.43)
mFSQ score, mean (SE)	61.5 (2.97)
MDS-UPDRS Part I (Nonmotor ADL), mean (SE)	18.6 (0.91)
MDS-UPDRS Part II (Motor ADL), mean (SE)	17.8 (1.40)
CGI-S score, mean (SE)	4.1 (0.05)
Suicidal Ideation at Baseline, C-SSRS	
Yes, n (%)	0 (0.0)
No, n (%)	29 (100%)
GDS score, mean (SE)	4.5 (0.5)
Schwab and England score (patient), mean (SE)	65.4 (2.74)
Schwab and England score (caregiver), mean (SE)	62.5 (2.85)

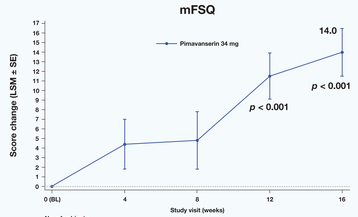
CGI-S, Clinical Global Impression–Severity of Illness; C-SSRS, Columbia-Suicide Severity Rating Scale; GDS, Geriatric Depression Scale; MDS-UPDRS, Movement Disorders Society–modified Unified Parkinson's Disease Rating Scale; mFSQ, Modified Functional Status Questionnaire; MMSE, Mini-Mental Status Examination; SE, standard error.

Table 2. Summary of TEAEs

Characteristic	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	–	–

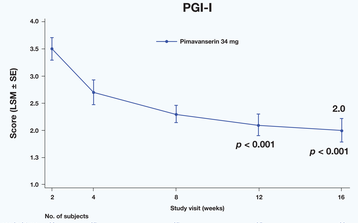
TEAE, treatment-emergent adverse event.
[a]Hyperuricemia (n = 1; 3.4%), syncope (n = 1; 3.4%); hypotension (n = 1; 3.4%).
[b]Electrocardiogram QT prolonged (n = 1; 3.4%).
[c]Squamous cell carcinoma (n = 1; 3.4%).

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



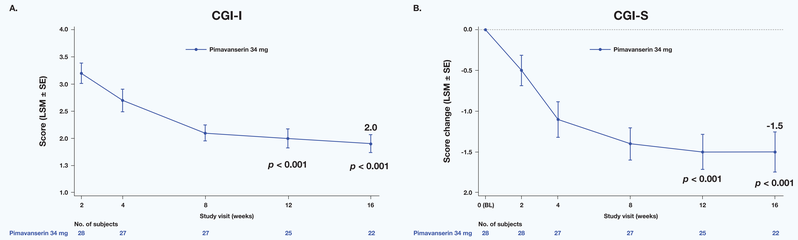
*Scale is standardized from 0-100; the baseline score was 61.5.
BL, baseline; LSM, least-squares means; SE, standard error.

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



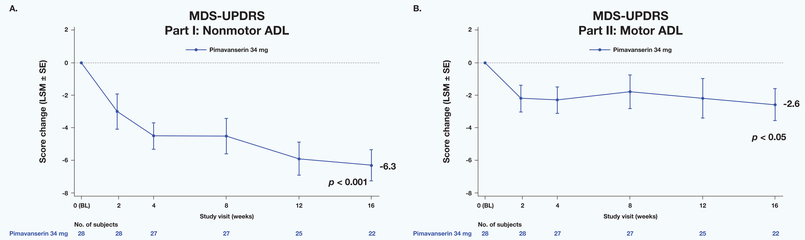
LSM, least-squared means; SE, standard error.

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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