Parkinson's Disease Related Outcomes among Newly Diagnosed Patients with Parkinson's Disease Psychosis Treated with Pimavanserin versus Other Atypical Antipsychotics and Quetiapine

Nazia Rashid[1], Krithika Rajagopalan[2], Daksha Gopal[2], Lambros Chrones[1]

[1]Medical Affairs, Acadia Pharmaceuticals Inc, San Diego, CA, USA; [2]Anlitiks Inc, Windermere, FL, USA

INTRODUCTION

- Parkinson's disease (PD) affects over 1 million individuals in the US; roughly 25—50% of patients develop Parkinson's disease psychosis (PDP), characterized by hallucinations and delusions (H&D).[1,2]
- Gait disturbances (GD) and cognitive impairment are features of PDP, driven by dopaminergic neurodegeneration, and are associated with increased risk of falls, injury, hospitalization and complicate disease management.[2-6]
- Pimavanserin (PIM) is the only FDA-approved AAP for the treatment of H&D associated with PDP and may have minimal impact on motor and cognition.[7]
- Despite this, off-label AAPs, most notably quetiapine (QUE), remain the most prescribed treatments for PDP.[5]

OBJECTIVES

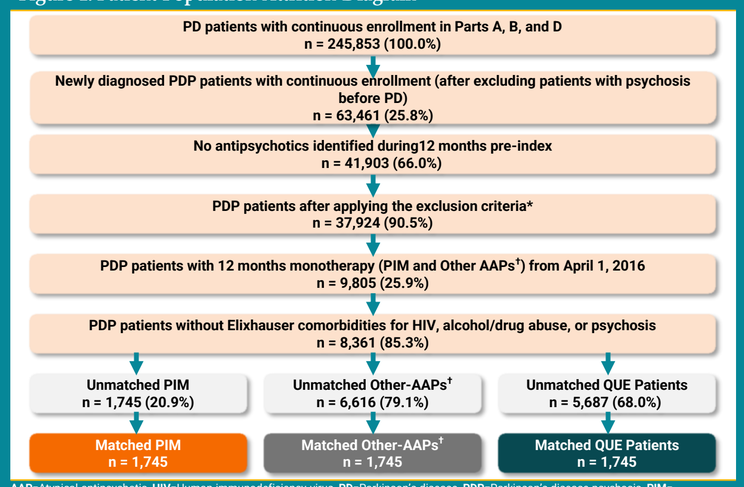
- To examine the rates of GD, cognitive impairment, and PD-related hospitalizations in community settings among Medicare beneficiaries with PDP who are treated with (i) PIM vs. Other-AAPs and (ii) PIM vs. QUE.

METHODS

Study Design & Data Source

- A retrospective database analysis of PDP patients was conducted using data from the 100% Medicare fee-for-service (FFS) sample of Parts A, B, and D claims (study period: 01/01/2013-12/31/2021).

Figure 1. Patient Population Attrition Diagram



AAP=Atypical antipsychotic, **HIV**=Human immunodeficiency virus, **PD**=Parkinson's disease, **PDP**=Parkinson's disease psychosis, **PIM**=Pimavanserin, **QUE**=Quetiapine. *Diagnosis of secondary parkinsonism, delirium, other psychotic disorders, alcohol-induced psychosis, drug-induced psychosis, schizophrenia, paranoia, or personality disorders †Patients treated with other-AAPs are limited to risperidone, olanzapine, aripiprazole, and quetiapine (clozapine, paliperidone, brexpiprazole excluded due to small numbers). **Note:** The attrition percentages reflect the relative change at each stage to previous step.

METHODS

Population & Cohort Identification	• PDP patients with ≥1 PD claim (ICD-9-CM: 332.0; ICD-10-CM: G20) and ≥1 psychosis claim (F06.0, F06.2, F22, F23, F28, F29, H53.16, R44.0, R44.1, R44.2, R44.3) between 1/1/2013 to 12/31/2021 who initiate 12-month continuous monotherapy on PIM, Other-AAPs, or QUE (index date) between 04/01/2016 and 12/31/2020. Date of first AAP prescription was defined as the index date.
Exclusion Criteria	• <12 months of continuous enrollment in pre- and post-index. • Diagnosis of psychosis before PD diagnosis. • Refer to Figure 1 for additional exclusion criteria.
Propensity Score Matching	• Patients on continuous PIM monotherapy were 1:1 propensity score matched on age, sex, race, geographic region, and 27 Elixhauser comorbidities to Other-AAPs or QUE using greedy nearest neighbor.
Baseline Patient Characteristics	• Age, sex, race, region, index year. • Dementia, insomnia, 27 of 31 Elixhauser comorbidities.
Study Outcomes	• Percentage of patients with ≥1 post-index GD or cognitive impairment and pre-post-index differences within each cohort (McNemar's test). • Percentage of patients with new-onset of GD and cognitive impairments among those with respective post-index complication. • Percent of PD-related hospitalizations post-index and adjusted risk ratios using log binomial models.

RESULTS

- Among 8,361 selected PDP patients who newly initiated an AAP, 20.87% (n=1,745) were on PIM and 79.13% (n=6,616) were on Other-AAPs, of whom 68.02% (n=5,687) comprised the QUE cohort (**Figure 1**).
- All three matched cohorts (n=1,745) had an approximate mean age of 77 years and were 55% male (**Table 1**). Baseline Elixhauser comorbidities were balanced across matched cohorts (**Table 2**).

Table 1. Matched Baseline Patient Demographics

Demographic Characteristic	PIM (n = 1,745)	Other-AAPs (n = 1,745)	QUE (n = 1,745)	SMD	
				PIM vs. Other-AAPs	PIM vs. QUE
Age in years					
Mean (SD)	77.18 (6.80)	77.21 (6.93)	77.30 (6.64)	0.004	0.017
Median (IQR)	77 (73, 82)	77 (73, 82)	77 (73, 82)		
Gender, n (%)					
Male	955 (54.73)	953 (54.61)	956 (54.79)	0.002	0.001
Female	790 (45.27)	792 (45.39)	789 (45.21)		
Race, n (%)					
White	1,580 (90.54)	1,603 (91.86)	1,603 (91.86)	0.047	0.047
Black	59 (3.38)	62 (3.55)	64 (3.67)	0.009	0.016
Asian	33 (1.89)	21 (1.20)	24 (1.38)	0.056	0.041
Other	25 (1.43)	30 (1.72)	28 (1.60)	0.023	0.014
Hispanic	14 (0.80)	14 (0.80)	11 (0.63)	0.000	0.020
Native American	8 (0.46)	2 (0.11)	3 (0.17)	0.064	0.051
Unknown	26 (1.49)	13 (0.74)	12 (0.69)	0.071	0.077
Geographic Region, n (%)					
South	744 (42.64)	740 (42.41)	736 (42.18)	0.005	0.009
Midwest	371 (21.26)	373 (21.38)	391 (22.41)	0.003	0.028
West	317 (18.17)	302 (17.31)	305 (17.48)	0.023	0.018
Northeast	313 (17.94)	330 (18.91)	313 (17.94)	0.025	0.000
Index Year, n (%)					
2016	184 (10.54)	392 (22.46)	378 (21.66)	0.325	0.306
2017	428 (24.53)	416 (23.84)	424 (24.30)	0.016	0.005
2018	357 (20.46)	373 (21.38)	366 (21.06)	0.023	0.013
2019	445 (25.50)	306 (17.54)	300 (17.19)	0.195	0.204
2020	331 (18.97)	258 (14.79)	277 (15.87)	0.112	0.082
Other Comorbidities, n (%)					
Dementia	1,442 (82.64)	1,525 (87.39)	1,532 (87.79)	0.134	0.146
Insomnia	659 (37.77)	816 (46.76)	818 (46.88)	0.183	0.185

AAPs=Atypical antipsychotics, **IQR**=Interquartile range, **PIM**=Pimavanserin, **QUE**=Quetiapine, **SD**=Standard deviation, **SMD**=Standardized mean difference.

Table 2. Matched Baseline Patient Comorbidities

Comorbidity	PIM (n = 1,745)	Other-AAPs (n = 1,745)	QUE (n = 1,745)	SMD	
				PIM vs. Other-AAPs	PIM vs. QUE
Other Neurological Disorders	1,714 (98.22)	1,711 (98.05)	1,712 (98.11)	0.013	0.009
Hypertension Uncomplicated	1,072 (61.43)	1,097 (62.87)	1,088 (62.35)	0.030	0.019
Depression	578 (33.12)	593 (33.98)	571 (32.72)	0.018	0.009
Cardiac Arrhythmia	347 (19.89)	354 (20.29)	366 (20.97)	0.010	0.027
Hypothyroidism	331 (18.97)	327 (18.74)	327 (18.74)	0.006	0.006
Peripheral Vascular Disorders	317 (18.17)	308 (17.65)	300 (17.19)	0.013	0.026
Fluid and Electrolyte Disorders	299 (17.13)	306 (17.54)	305 (17.48)	0.011	0.009
Diabetes Uncomplicated	295 (16.91)	327 (18.74)	324 (18.57)	0.048	0.044
Hypertension Complicated	228 (13.07)	216 (12.38)	212 (12.15)	0.021	0.028
Diabetes Complicated	206 (11.81)	228 (13.07)	228 (13.07)	0.038	0.038
Renal Failure	199 (11.40)	222 (12.72)	215 (12.32)	0.040	0.028
Chronic Pulmonary Disease	196 (11.23)	182 (10.43)	231 (13.24)	0.026	0.061
Congestive Heart Failure	178 (10.20)	148 (8.48)	146 (8.37)	0.059	0.063
Valvular Disease	160 (9.17)	161 (9.23)	146 (8.37)	0.002	0.028
Weight Loss	137 (7.85)	116 (6.65)	130 (7.45)	0.046	0.015
Deficiency Anemia	133 (7.62)	131 (7.51)	132 (7.56)	0.004	0.002
Solid Tumors w/o Metastasis	129 (7.39)	160 (9.17)	145 (8.31)	0.064	0.034
Obesity	103 (5.90)	122 (6.99)	113 (6.48)	0.044	0.024
RA/CVD	66 (3.78)	79 (4.53)	73 (4.18)	0.037	0.021
Coagulopathy	66 (3.78)	68 (3.90)	71 (4.07)	0.006	0.015
Pulmonary Circulation Disorders	50 (2.87)	54 (3.09)	48 (2.75)	0.013	0.007
Liver Disease	22 (1.26)	24 (1.38)	24 (1.38)	0.010	0.010
Paralysis	22 (1.26)	14 (0.80)	12 (0.69)	0.045	0.058
Blood Loss Anemia	17 (0.97)	23 (1.32)	25 (1.43)	0.032	0.042
Lymphoma	15 (0.86)	14 (0.80)	16 (0.92)	0.006	0.006
Peptic Ulcer Disease*	11 (0.63)	17 (0.97)	16 (0.92)	0.039	0.033
Metastatic Cancer	9 (0.52)	12 (0.69)	14 (0.80)	0.022	0.035

AAPs=Atypical antipsychotics, **PIM**=Pimavanserin, **QUE**=Quetiapine, **RA/CVD**=Rheumatoid Arthritis/Collagen Vascular Diseases, **SMD**=Standardized mean difference.*Excluding bleeding.

- Post-index rates of PD-related hospitalizations were lower among PIM (16.73%) cohort compared to Other-AAPs (18.62%) and QUE (18.85%). The adjusted risk ratios (95% CI) for PIM vs. Other-AAPs and PIM vs. QUE were similar [0.93 (0.80, 1.07)].

- Rates of GD did not increase significantly following PIM initiation; however, increases were observed among Other-AAPs and QUE. Among patients with post-index GD, a lower proportion of new patients developed GD post-index in the PIM cohort compared to Other-AAPs and QUE (**Figure 2**).
- Rates of cognitive impairment did not increase significantly after initiating PIM; whereas increases were observed among Other-AAPs and QUE. Among patients with post-index cognitive impairment, a lower proportion of new patients developed cognitive impairments post-index in the PIM cohort compared to Other-AAPs and QUE (**Figure 3**).

Figure 2. Pre-Post Analysis of Gait Disturbances

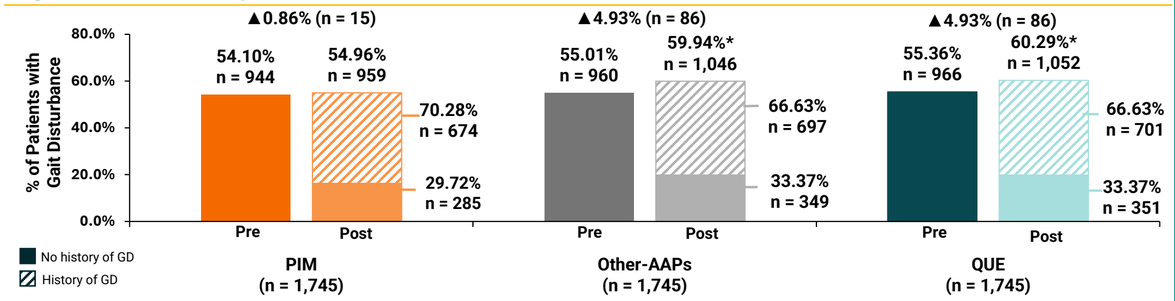
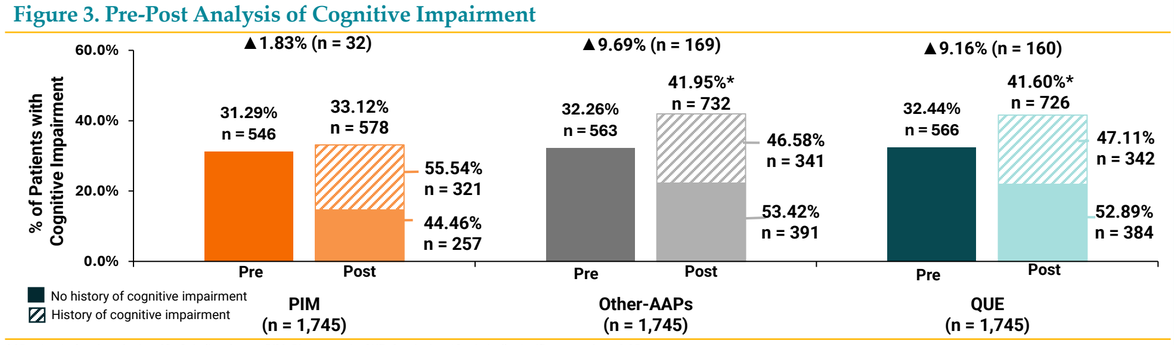


Figure 3. Pre-Post Analysis of Cognitive Impairment



AAPs=Atypical antipsychotics, **GD**=Gait disturbance, **PIM**=Pimavanserin, **QUE**=Quetiapine. *Statistically significant, p-value < 0.05.

Limitations

- As with any administrative claims data analysis, this study may contain coding errors, missed claims, and potential biases introduced by data omissions. Since the identification of PDP was based on a diagnosis of psychosis, hallucinations, or delusions - as there is no diagnostic code for PDP - it is likely that PDP diagnosis is underestimated. Potential for residual confounding may exist despite matching and covariate adjustment.

CONCLUSIONS

- **PIM showed minimal-to-no worsening of GD and cognitive impairment following treatment initiation, whereas Other-AAPs, including QUE were associated with significant increases in both outcomes.**
- **PIM patients were 7% less likely to experience PD-related hospitalizations, though this finding was not significant.**
- **A lower proportion of PIM patients developed new-onset of gait disturbances and cognitive impairments in the post-index period compared to Other-AAPs and QUE, suggesting that PIM may offer a more favorable neuromotor and cognitive risk profile for PDP patients.**
- **These findings may support the role of PIM as a treatment option that limits functional decline in patients living with PDP, warranting further investigation into its long-term effects on gait and cognition.**

REFERENCES

1. Willis AW et al. *NPJ Parkinsons Dis*. 2022;8(1):170. 2. Fénelon G & Alves G. *J Neurol Sci*. 2010;289(1-2):12-17. 3. Forns J et al. *PLoS One.* 2021;16(1):e0246121. 4. Kelly VE et al. *Parkinsons Dis*. 2012;2012:918719. 5. Weintraub D & Burn DJ. *Mov Disord.* 2011;26(6):1022-1031. 6. Rashid N et al. *J Comp Eff Res*. 2025;14(12):e250129. 7. Nuplazid (pimavanserin). Package insert. Acadia Pharmaceuticals Inc; 2025.

ACKNOWLEDGMENTS

Development of this poster was supported by Safiuddin Shoeb Syed, Demetrios Spaccavento, and Ritu Pathak, employees of Anlitiks Inc.

DISCLOSURES

The study was supported by Acadia Pharmaceuticals Inc. (San Diego, CA, USA).

ACADIA®