Patients with Parkinson's Disease Psychosis and Dementia: Analysis of Healthcare Resource Utilization and Time to Long Term Care Admission among US Medicare Beneficiaries Initiating Pimavanserin versus Other-Atypical Antipsychotics

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INTRODUCTION

- Research suggests that hallucinations and delusions among patients with Parkinson's disease (PD) psychosis (PDP) may exacerbate cognitive decline, thereby accelerating the occurrence and worsening of dementia.[1]
- The co-occurrence of psychosis and dementia severely affects the quality of life for both PDP patients and their caregivers.[2,3]
- Pimavanserin (PIM) is the only FDA-approved atypical antipsychotic (AAP) for the treatment of hallucinations and delusions associated with PDP.[4]
- However, other-AAPs such as quetiapine, risperidone, olanzapine, and aripiprazole are commonly prescribed off-label.[5]
- Real-world data on healthcare resource utilization (HCRU) and time to long term care admissions (LTCA) among PIM vs. other-AAPs treated patients with co-existing dementia with PDP diagnosis (PDP+D) are needed.

OBJECTIVES

- To compare rates of all-cause and psychiatric-related HCRU and to assess the time to LTCA among PDP patients treated with PIM vs. other-AAPs with co-existing dementia in a real-world setting.

METHODS

Study Design and Data Source

- A retrospective analysis was conducted using Parts A, B, and D claims from a 100% Medicare sample of PDP+D patients from April 2015 to December 2021 (study period).

Study Population

- ***Inclusion Criteria:*** Treatment-naïve PDP+D patients initiating (i.e., index date) continuous monotherapy of PIM or other-AAPs for ≥12-months during April 2016 to December 2020 without any prior-AAPs use during the 12-month pre-index period were selected.
- ***Exclusion Criteria:*** Patients with a pre-index diagnosis of secondary parkinsonism, delirium, other psychotic disorders, alcohol/drug-induced psychosis, schizophrenia, paranoia, or personality disorders.

Study Measures & Outcomes

- ***Demographics:*** Age, sex, race, geographic region and comorbidities.
- ***HCRU Measures (12-month follow-up):***
  - Rates of all-cause and psychiatric (psych)-related inpatient hospitalizations (IP) [including type of stay: short-term (ST) stay, long-term (LT) stay, or skilled nursing facility (SNF) stay].
  - Rates of all-cause and psychiatric-related emergency room (ER) visits.
  - Rates of all-cause and psychiatric-related office visits (OV) and outpatient visits (OP).
- ***Time to LTCA:*** LTCA was defined as a composite of SNF-stay or LT-stay.

Statistical Methods

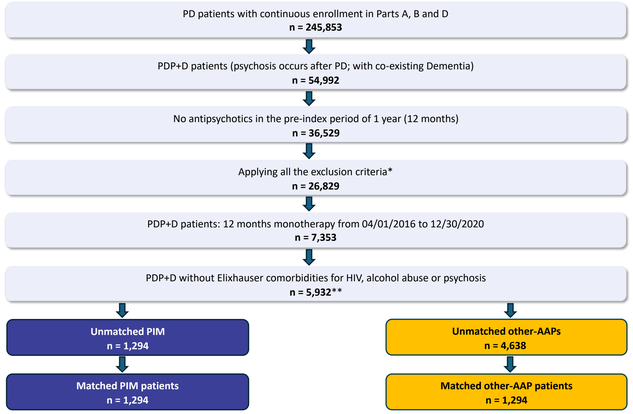
- ***Matching:*** Patients on PIM vs. other-AAPs were 1:1 propensity score-matched (PSM) on 31 variables (age, sex, race, region, and 27 Elixhauser comorbidity characteristics), with covariate balance assessed using standardized mean differences (SMD).
- ***Descriptive Statistics:*** Frequencies and percentages were reported for categorical variables; mean, median, and range for continuous variables. Chi-square tests were used for categorical variables, while T-tests and Wilcoxon Rank Sum tests assessed differences in continuous outcomes between PIM and other-AAPs.
- ***HCRU Differences:*** Evaluated using log binomial regressions adjusted for patient demographics and comorbidities; relative risks (RR) and 95% confidence intervals (95% CI) were reported.
- ***Time to LTCA (days):*** Assessed using Kaplan-Meier curves, with log-rank tests comparing differences between groups. Hazard ratios (HR) and 95% CIs were estimated via Cox proportional hazard model to assess the risk among PIM vs. other-AAPs treated patients.
- Analyses were performed using SAS® Enterprise Server via the CMS Virtual Research Data Center.

RESULTS

Demographic and Clinical Characteristics

- A total of 5,932 patients met our study inclusion and exclusion criteria. This population included 1,294 unmatched PDP+D patients on PIM monotherapy and 4,638 on other-AAP monotherapy.
- After 1:1 matching, the final sample consisted of 1,294 patients on PIM and 1,294 on other-AAPs (Figure 1).

Figure 1: Patient Attrition Population Selection



*Diagnosis of secondary parkinsonism, delirium, other psychotic disorder, alcohol/drug-induced psychosis, schizophrenia, paranoia, or personality disorders. **Patients treated with other-AAPs in unmatched were limited to risperidone (n = 242), olanzapine (n = 147), aripiprazole (n = 118), and quetiapine (n = 4131); among the matched group other-AAPs included risperidone (n = 58), olanzapine (n = 40), aripiprazole (n = 22), and quetiapine (n = 1174); clozapine, paliperidone, brexpiprazole were excluded due to small numbers.

Abbreviations: AAPs, Atypical anti-psychotics; PD, Parkinson's disease; PDP, Parkinson's disease psychosis, PDP+D, Parkinson's disease psychosis with Dementia; PIM, Pimavanserin, other-AAPs, other-atypical antipsychotics; HIV, Human immunodeficiency virus

Table 1: Baseline Demographics and Clinical Characteristics after Matching

Characteristics	PIM (n = 1,294)	other-AAPs (n = 1,294)	SMD
Age (in years)			
Mean (SD)	77.34 (6.75)	77.61 (6.74)	0.040
Median (IQR)	77 (73, 82)	78 (73, 82)	
Male, n(%)	726 (56.11%)	718 (55.49%)	0.012
Race, n (%)			
White	1,179 (91.11%)	1,190 (91.96%)	0.031
Black	36 (2.78%)	370 (2.86)	0.005
Asian	25 (1.93%)	12 (0.93%)	0.085
Hispanic	10 (0.77%)	10 (0.77%)	0.000
North American Native	7 (0.54%)	6 (0.46%)	0.011
others	18 (1.39%)	19 (1.47%)	0.007
Unknown	19 (1.47%)	20 (1.55%)	0.006
Region, n (%)			
South	522 (40.34%)	513 (39.64%)	0.014
Midwest	280 (21.64%)	283 (21.87%)	0.006
Northeast	246 (19.10%)	53 (19.55%)	0.014
West	246 (19.10%)	245 (18.93%)	0.002
Comorbidities, n (%)			
Insomnia	575 (44.44%)	583 (45.05%)	0.012

Abbreviations: PIM, Pimavanserin; other-AAPs, other-atypical antipsychotics; SD, Standard deviation; IQR, Interquartile range; SMD, Standardized mean difference

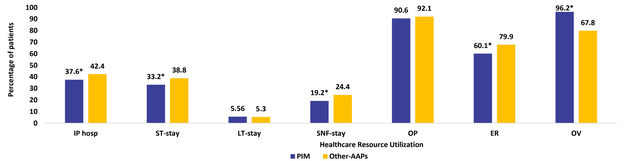
- A SMD value <0.1 means that there is no difference between the groups; The groups were well balanced in Table 1 after PSM.

Table 2: Baseline Clinical Comorbidities after Matching

Comorbidities, n (%)	PIM (n = 1,294)	Other-AAPs (n = 1,294)	SMD
Blood Loss Anemia	13 (1.0%)	11 (0.8%)	0.016
Cardiac Arrhythmia	271 (20.9%)	274 (21.1%)	0.006
Chronic Pulmonary Disease	152 (11.7%)	173 (13.3%)	0.049
Coagulopathy	57 (4.4%)	58 (4.4%)	0.004
Congestive Heart Failure	134 (10.3%)	141 (10.9%)	0.018
Deficiency Anemia	104 (8.0%)	106 (8.2%)	0.006
Depression	467 (36.1%)	476 (36.8%)	0.014
Diabetes Complicated	155 (11.9%)	140 (10.8%)	0.036
Diabetes Uncomplicated	225 (17.4%)	209 (16.1%)	0.033
Fluid and Electrolyte Disorders	238 (18.4%)	231 (17.8%)	0.014
Hypertension Complicated	186 (14.3%)	163 (11.6%)	0.052
Hypertension Uncomplicated	843 (65.1%)	835 (64.5%)	0.013
Hypothyroidism	273 (21.1%)	268 (20.1%)	0.010
Liver Disease	13 (1.0%)	18 (1.3%)	0.036
Lymphoma	13(1.0%)	17 (1.3%)	0.013
Metastatic Cancer	10 (0.7%)	14 (1.0%)	0.029
Obesity	79 (6.1%)	68 (5.2%)	0.037
Other Neurological Disorders	1,282 (99.0%)	1,282 (99.0%)	0.000
Paralysis	17 (1.3%)	9 (0.7%)	0.062
Peptic ulcer excluding bleeding	8 (0.6%)	10 (0.7%)	0.019
Peripheral Vascular Disease	261 (20.1%)	262 (20.2%)	0.002
Pulmonary Circulation Disorder	32 (2.4%)	47 (3.6%)	0.067
Renal Failure	161 (12.4%)	145 (11.2%)	0.038
Rheumatoid Arthritis	44 (3.4%)	41 (3.1%)	0.032
Solid Tumors without Metastasis	103 (7.9%)	122 (9.4%)	0.052
Valvular Disease	126 (9.7%)	131 (10.1%)	0.013
Weight Loss	117 (9.0%)	143 (11.0%)	0.067

- Clinical characteristics and descriptive statistics for the 1:1 matched groups are described in Tables 1&2. Both PIM cohorts appeared to have similar mean age, gender and comorbidity profile after matching.

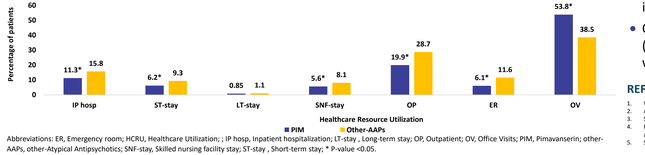
Figure 2: Rates of All-Cause Health Care Resource Utilization



Abbreviations: ER, Emergency room; HCRU, Healthcare Utilization; IP hosp, Inpatient hospitalization; LT-stay , Long-term stay; OP, Outpatient; OV, Office Visits; PIM, Pimavanserin; other-AAPs, other-Atypical Antipsychotics; SNF-stay, Skilled nursing facility stay; ST-stay, Short-term stay; * P-value <0.05.

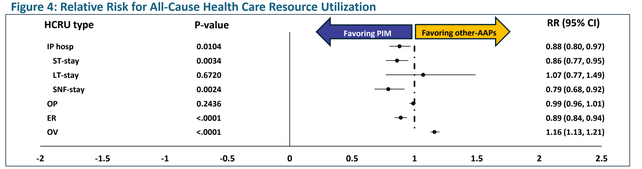
- Patients on PIM reported lower all-cause HCRU vs. other-AAPs for any (≥1) IP hospitalizations (37.6% vs. 42.4%, p<0.05), and by type of IP hospitalizations [ST-stays (33.2% vs. 38.8%, p<0.05), LT-stays (5.6% vs. 5.3%, p=0.67), SNF-stays (19.2% vs. 24.4%, p<0.05)], OP visits (90.6% vs. 92.1%, p=0.24), and ER visits (60.1% vs. 67.8%, p<0.05), Figure 2.
- Rates of pscyh-related visits were lower for PIM vs. other-AAPs; IP hospitalizations (11.3% vs. 15.8%, p<0.05), ER visits (6.1% vs. 11.6%, p<0.05), Figure 3.
- Patients on PIM also had a lower relative risk for all-cause HCRU across all settings except LT-stays and office visits, Figure 4; patients on PIM also had a lower relative risk for psych-related HCRU across all settings except OV, Figure 5.

Figure 3: Rates of Psych-Related Health Care Resource Utilization



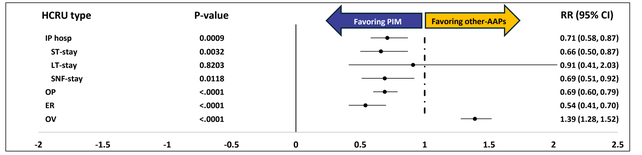
Abbreviations: ER, Emergency room; HCRU, Healthcare Utilization; , IP hosp, Inpatient hospitalization; LT-stay , Long-term stay; OP, Outpatient; OV, Office Visits; PIM, Pimavanserin; other-AAPs, other-Atypical Antipsychotics; SNF-stay, Skilled nursing facility stay; ST-stay , Short-term stay; * P-value <0.05.

Figure 4: Relative Risk for All-Cause Health Care Resource Utilization



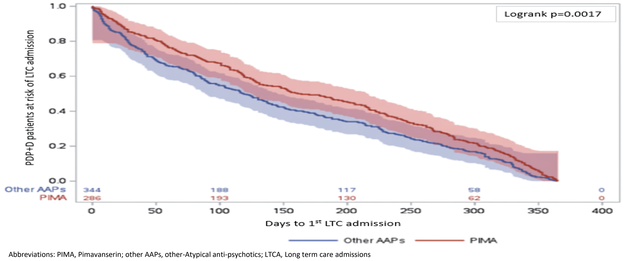
Abbreviations: AAPs, Atypical anti-psychotics; ER, Emergency room; HCRU, Health care resource utilization; IP hosp, Inpatient hospitalization; ST-stay, Short-term stay; LT-stay, Long-term stay; OP, Outpatient; OV, Office visit; PIM, Pimavanserin; other-AAPs, other-atypical antipsychotics; SNF, Skilled nursing facility; RR, Relative risk.

Figure 5: Relative Risk for Psych-Related Health Care Resource Utilization



Abbreviations: AAPs, Atypical anti-psychotics; ER, Emergency room; HCRU, Health care resource utilization; IP hosp, Inpatient hospitalization; ST-stay, Short-term stay; LT-stay, Long-term stay; OP, Outpatient; OV, Office visit; PIM, Pimavanserin; other-AAPs, other-atypical antipsychotics; SNF-stay, Skilled nursing facility stay; RR, Relative risk.

Figure 6: Time to Long Term Care Admissions



Abbreviations: PIMA, Pimavanserin; other AAPs, other-Atypical anti-psychotics; LTCA, Long term care admissions

- Patients on PIM had lower LTCA (22.1% vs. 26.7%, p<0.05) and greater median days to LTCA [163 (65, 284) vs. 119 (39, 248), p<0.05)] compared to patients on other AAPs.
- Patients on PIM also had a 23% lower risk of LTCA [HR (95% CI) =0.77 (0.66, 0.90), (p=0.0017)] compared to patients on other AAPs, Figure 6.

CONCLUSIONS

- PDP+D patients on PIM-monotherapy demonstrated lower rates and lower relative risk for all-cause and psych-related IP hospitalizations and ER visits compared to those on other-AAP monotherapy.
- PDP+D patients on PIM monotherapy had a 23% lower risk of LTCA and experienced a 44-day longer delay in being admitted to LTCA compared to those on other-AAP monotherapy.
- Our results are consistent with prior research that showed PIM vs. other-AAPs lowered HCRU outcomes (e.g., all-cause and psych-related IP hospitalizations, ER visits) in real-world settings among PDP patients with or without dementia.

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