Real-World Persistence on Olanzapine/Samidorphan Versus Other Oral Second-Generation Antipsychotics in Patients With Schizophrenia

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BACKGROUND

- Poor persistence and adherence to oral antipsychotic medications are common in clinical practice and are associated with increased risk of relapse[1,2]
- Treatment persistence represents a global measure of effectiveness that reflects a medication's efficacy, safety, and tolerability, from both patients' and clinicians' perspectives[3]
- In prior real-world studies of adults with schizophrenia or bipolar I disorder, the combination of olanzapine and samidorphan (OLZ/SAM) was associated with greater adherence, longer persistence, and fewer disease-related acute care events (proxies for relapse) vs olanzapine[4,5]

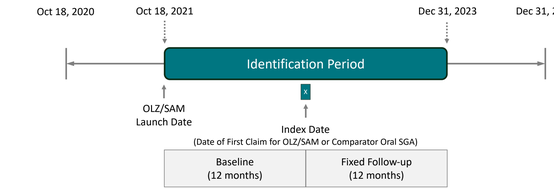
OBJECTIVE

- To evaluate real-world persistence and adherence with OLZ/SAM compared with other oral second-generation antipsychotic (SGA) medications among patients with schizophrenia

METHODS

- This retrospective claims analysis used Komodo Healthcare Map data (10/18/2020–12/31/2024)
- Data from Medicaid-insured adults with ≥1 medical claim with a diagnosis of schizophrenia during the baseline or follow-up period and ≥1 claim for OLZ/SAM or a comparator oral SGA (aripiprazole, brexpiprazole, cariprazine, lumateperone, lurasidone, olanzapine, or risperidone) during the identification period were included
  - Date of the first observed pharmacy or medical claim for OLZ/SAM or one of the comparator SGAs (index medication) was defined as the index date; OLZ/SAM claims were prioritized to set the index date
- Inverse probability treatment weighting, a propensity score–based method, was used to balance cohorts on key demographic and clinical variables
- Outcomes assessed included
  - Persistence rate: proportion of patients who continued the index medication for the full 12-month study period
  - Duration of persistence: days from index date to discontinuation date (using a ≥45-day gap to define treatment discontinuation) or to end of the follow-up period
  - Adherence: measured as medication possession ratio ([MPR] ≥0.80); MPR was calculated as the sum of the dispensed days' supply of the index medication in the follow-up period divided by the number of days in the follow-up period
- *P* values ≤0.05 were considered statistically significant

Figure 1. Study Design



OLZ/SAM, combination olanzapine and samidorphan; SGA, second-generation antipsychotic.

RESULTS

- A total of 45,566 patients with schizophrenia were included (OLZ/SAM, n=1244; aripiprazole, n=11,995; brexpiprazole, n=421; cariprazine, n=1650; lumateperone, n=423; lurasidone, n=2030; olanzapine, n=14,630; risperidone, n=13,173)
- Comparisons to brexpiprazole (n=421) and lumateperone (n=423) were not assessed due to the relatively low numbers of patients treated with these medications vs OLZ/SAM
- After weighting, all treatment cohorts were balanced on key baseline demographic and clinical variables (**Tables 1** and **2**)
- Patients initiating OLZ/SAM vs other oral SGAs were significantly more likely to remain on treatment at 12 months (odds ratio [OR] range, 1.57–2.71; all *P*<0.001) (**Figure 2**)
- Mean (SD) duration of treatment persistence was significantly longer with OLZ/SAM (201.8 [143.6] days) vs all comparators (range, 132.1 [129.5] to 174.1 [138.8] days; all *P*<0.001) (**Figure 3**)
- At least 50% of OLZ/SAM patients remained on treatment for ≥180 days (median persistence) vs median durations of 67–121 days for comparator oral SGAs (**Figure 3**)
- Patients initiating OLZ/SAM vs comparator oral SGAs were also twice as likely to be adherent (MPR ≥0.80 OR range, 1.33–2.53; all *P*<0.01) (**Figure 4**)

RESULTS (cont'd)

Table 1. Weighted Baseline Patient Demographics

Characteristics	OLZ/SAM (n=1244)	Aripiprazole (n=11,995)	Cariprazine (n=1650)	Lurasidone (n=2030)	Olanzapine (n=14,630)	Risperidone (n=13,173)
Age group, n (%)						
18–24 years	157 (12.6)	1494 (12.5)	223 (13.5)	254 (12.5)	1843 (12.6)	1673 (12.7)
25–34 years	412 (33.1)	3961 (33.0)	554 (33.6)	679 (33.4)	4755 (32.5)	4348 (33.0)
35–44 years	346 (27.8)	3370 (28.1)	444 (26.9)	570 (28.1)	4152 (28.4)	3657 (27.8)
45–54 years	175 (14.1)	1687 (14.1)	228 (13.8)	276 (13.6)	2047 (14.0)	1850 (14.0)
55–64 years	145 (11.7)	1369 (11.4)	185 (11.2)	235 (11.6)	1641 (11.2)	1492 (11.3)
≥65 years	9 (0.7)	114 (1.0)	15 (0.9)	16 (0.8)	192 (1.3)	152 (1.2)
Female, n (%)	590 (47.4)	5717 (47.7)	794 (48.1)	981 (48.3)	6945 (47.5)	6200 (47.1)
Region, n (%)						
West	455 (36.6)	4445 (37.1)	602 (36.5)	744 (36.7)	5521 (37.7)	5007 (38.0)
South	338 (27.2)	3242 (27.0)	444 (26.9)	566 (27.9)	3972 (27.1)	3507 (26.6)
Midwest	275 (22.1)	2664 (22.2)	372 (22.5)	452 (22.3)	3168 (21.7)	2857 (21.7)
Northeast	176 (14.1)	1641 (13.7)	232 (14.1)	267 (13.2)	1967 (13.4)	1798 (13.6)
Other	0	3 (0.02)	1 (0.03)	1 (0.05)	2 (0.01)	3 (0.03)

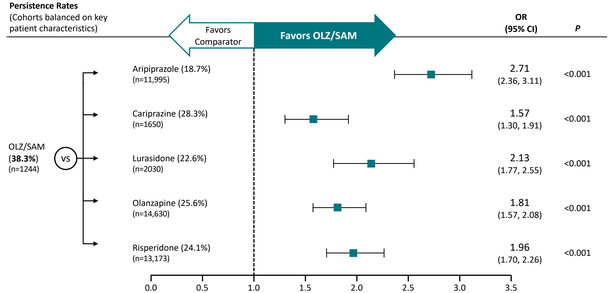
OLZ/SAM, combination olanzapine and samidorphan.

Table 2. Weighted Baseline Clinical Characteristics

Characteristics	OLZ/SAM (n=1244)	Aripiprazole (n=11,995)	Cariprazine (n=1650)	Lurasidone (n=2030)	Olanzapine (n=14,630)	Risperidone (n=13,173)
Charlson Comorbidity Index category, n (%)						
0	825 (66.3)	7979 (66.5)	1103 (66.8)	1341 (66.1)	9699 (66.3)	8775 (66.6)
1–2	318 (25.6)	3054 (25.5)	425 (25.8)	522 (25.7)	3751 (25.6)	3364 (25.5)
3–4	77 (6.2)	682 (5.7)	93 (5.6)	115 (5.7)	781 (5.3)	760 (5.8)
≥5	24 (1.9)	280 (2.3)	29 (1.8)	52 (2.6)	399 (2.7)	274 (2.1)
Comorbid conditions, n (%)						
Anxiety disorder	636 (51.1)	6131 (51.1)	884 (53.6)	1046 (51.5)	7547 (51.6)	6793 (51.6)
Obesity	513 (41.2)	4978 (41.5)	665 (40.3)	834 (41.1)	6092 (41.6)	5453 (41.4)
Any substance use disorder	497 (40.0)	4750 (39.6)	670 (40.6)	821 (40.4)	5751 (39.3)	5173 (39.3)
Major depressive disorder	448 (36.0)	4255 (35.5)	603 (36.5)	731 (36.0)	5230 (35.7)	4735 (35.9)
Hypertension	428 (34.4)	4086 (34.1)	554 (33.6)	694 (34.2)	5031 (34.4)	4475 (34.0)
Hyperlipidemia	403 (32.4)	3850 (32.1)	511 (31.0)	638 (31.4)	4680 (32.0)	4224 (32.1)
Posttraumatic stress disorder	249 (20.0)	2434 (20.3)	355 (21.5)	435 (21.4)	3043 (20.8)	2738 (20.8)
Type 2 diabetes	231 (18.6)	2201 (18.3)	321 (19.5)	379 (18.7)	2719 (18.6)	2423 (18.4)
Alcohol use disorder	230 (18.5)	2201 (18.3)	310 (18.8)	368 (18.1)	2640 (18.0)	2363 (17.9)
Intentional self-inflicted injury	151 (12.1)	1442 (12.0)	208 (12.6)	247 (12.2)	1749 (12.0)	1596 (12.1)
Medication use during baseline period, n (%)						
Any non–index antipsychotic	729 (58.6)	7116 (59.3)	1012 (61.3)	1215 (59.9)	8700 (59.5)	7858 (59.7)
Any other behavioral health medication	1122 (90.2)	10,838 (90.4)	1499 (90.8)	1835 (90.4)	13,236 (90.5)	11,920 (90.5)
Any other medication	723 (58.1)	6984 (58.2)	955 (57.9)	1165 (57.4)	8562 (58.5)	7728 (58.7)

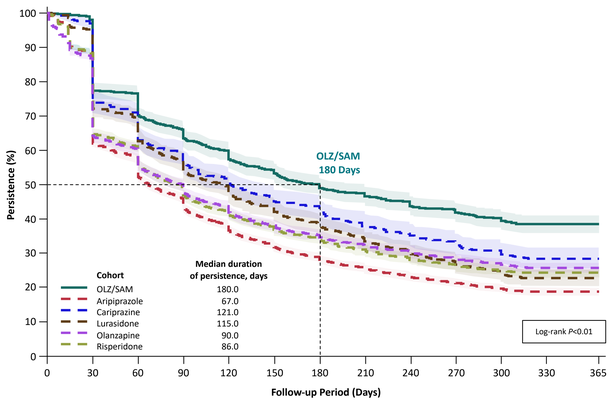
OLZ/SAM, combination olanzapine and samidorphan.

Figure 2. Persistence Rates[a] With Index Medication During 12-Month Follow-up: OLZ/SAM vs Comparator Oral SGAs[b]



[a]Persistence rate was defined as the proportion of patients who continued the index medication for the full 12-month follow-up period (did not discontinue).
[b]Given lower sample sizes for brexpiprazole (persistence rate, 29.0%; n=421) and lumateperone (persistence rate, 2.8%; n=423), data are not compared with OLZ/SAM.
OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio; SGA, second-generation antipsychotic.

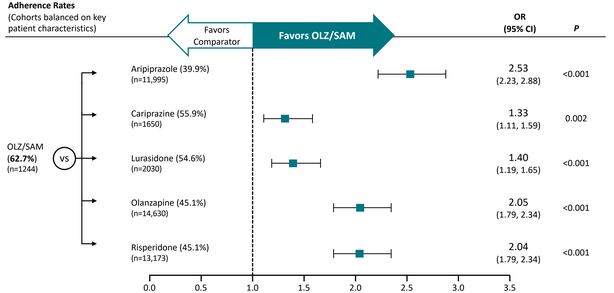
Figure 3. Kaplan-Meier Curves of Probability of Persistence[a]



	OLZ/SAM (n=1244)	Aripiprazole (n=11,995)	Cariprazine (n=1650)	Lurasidone (n=2030)	Olanzapine (n=14,630)	Risperidone (n=13,173)
Persistence,[b] mean (SD), days	201.8 (143.6)	132.1 (129.5)*	174.1 (138.8)*	160.6 (132.5)*	151.0 (141.4)*	147.9 (138.0)*

*P<0.01.
[a]Duration of persistence measured as the number of days from the index date to the discontinuation date (for patients who discontinued) or from the index date to the end of the follow-up period (for patients who did not discontinue).
[b]Given lower sample sizes for brexpiprazole (mean [SD] duration of persistence, 170.0 days [138.7]; n=421) and lumateperone (mean [SD] duration of persistence, 95.0 days [79.3]; n=423), data are not compared with OLZ/SAM.
OLZ/SAM, combination olanzapine and samidorphan.

Figure 4. Adherence (MPR ≥0.80) Rates[a] With Index Medication During 12-Month Follow-up: OLZ/SAM vs Comparator Oral SGAs[b]



[a]MPR was calculated as the sum of the dispensed days' supply of the index medication in the follow-up period divided by the number of days in the follow-up period.
[b]Given lower sample sizes for brexpiprazole (adherence rate, 58.9%; n=421) and lumateperone (adherence rate, 45.2%; n=423), data are not compared with OLZ/SAM.
MPR, medication possession ratio; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio; SGA, second-generation antipsychotic.

Clinical Context

In this retrospective claims analysis, OLZ/SAM was associated with more favorable treatment patterns vs comparator oral SGAs[a]

~2 times more likely to **stay on treatment**[b]
Persistence Rate
odds ratio range vs comparator oral SGAs **1.57–2.71, all *P*<0.001**

50% stayed on treatment **≥6 months**
Duration of Persistence
vs 2–4 months for comparator oral SGAs

~2 times more likely to stay **adherent to treatment**[b]
Treatment adherence
odds ratio range vs comparator oral SGAs **1.33–2.53, all *P*<0.01**

[a]Versus aripiprazole, cariprazine, lurasidone, olanzapine, and risperidone; given lower sample sizes for brexpiprazole (n=421) and lumateperone (n=423), data are not compared with OLZ/SAM.
[b]Based on odds ratios for persistence and adherence; corresponds to approximately 2-fold higher likelihood of remaining on OLZ/SAM treatment vs comparator oral SGAs during the 12-month follow-up period.
OLZ/SAM, combination olanzapine and samidorphan; SGA, second-generation antipsychotic.

LIMITATIONS

- The insured group studied may not be representative of uninsured patients or those insured but not by Medicaid
- Claims data do not capture disease severity and may be subject to data omissions and/or coding inaccuracies
- Presence of a claim for a filled prescription may not indicate that the medication was consumed
- Due to the fixed follow-up time, treatment patterns and acute care events reported may not fully capture the effects of longer-term (>12 months) OLZ/SAM or comparator oral SGA use
- Although the study adjusted for many known potential confounders, other clinical measures that may act as additional confounders are not available in administrative claims data
- No adjustment for multiplicity was performed for the statistical tests used in these analyses

CONCLUSIONS

- In this retrospective analysis of claims data in patients with schizophrenia, OLZ/SAM was associated with a statistically significantly higher persistence rate, longer duration of persistence, and better adherence during 12 months of follow-up vs comparator oral SGAs
- Compared with other oral SGAs, patients on OLZ/SAM were 57%–171% more likely to remain on treatment over 12 months
- Patients on OLZ/SAM were also 33%–153% more likely to meet the adherence threshold (MPR ≥0.80) vs comparator oral SGAs
- Overall, these findings suggest improved treatment continuity with OLZ/SAM vs comparator oral SGAs
- In clinical practice, sustained treatment continuity may reflect a favorable balance between efficacy and tolerability and patient satisfaction and acceptance[3]

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DISCLOSURES

AJC has been a consultant or on an advisory board for AbbVie, Acadia, Actinogen, Alfasigma, Alkermes, Anavex Life Sciences, Arrivo BioVentures, Autobahn Therapeutics, Axsome, Aytu Biopharma, BioXcel, Boehringer Ingelheim, Bristol Myers Squibb, Collegium Pharmaceutical, Corium, Definium Therapeutics, Delpor, 4M Therapeutics, Helus Pharma, Incannex Healthcare, Intra-Cellular Therapies, J&J Innovative Medicine, Jazz Pharma, Knight Therapeutics, Kye Pharmaceuticals, Kuvatris Therapeutics, LivaNova, Lundbeck, Luye Pharma, MapLight Therapeutics, Mentavi, Neumora, Neurocrine Biosciences, NeuroSigma, Noven, Otsuka, Relmada, Sensorium Therapeutics, Sirtsei Pharmaceuticals, Supernus, Teva, Thynk, Transneural Therapeutics, Tris Pharma, Vanda Pharmaceuticals, and Vistagen; is on the speakers' bureau for AbbVie, Alfasigma, Alkermes, Axsome, Aytu Biopharma, Boehringer Ingelheim, Bristol Myers Squibb, Collegium Pharmaceutical, Corium, Intra-Cellular Therapies, J&J Innovative Medicine, Knight Therapeutics, Kye Pharmaceuticals, Lundbeck, Luye Pharma, Neurocrine Biosciences, Noven, Otsuka, Supernus, Teva, Tris Pharma, and Vanda Pharmaceuticals; serves on a data safety monitoring board for Compass Pathways; and holds stock options/equity from EMA Wellness, Evolution Research Group, 4M Therapeutics, and Transneural Therapeutics.

CUC has been a consultant and/or advisor for or has received honoraria from AbbVie, Alkermes, Allergan, Angelini, Aristo, Autobahn, Boehringer-Ingelheim, Bristol Myers Squibb, Cardio Diagnostics, Cerevel, CNX Therapeutics, Compass Pathways, Darnitsa, Delpor, Denovo, Draig, Eli Lilly, EuMentis Therapeutics, Gedeon Richter, GH Research, Hikma, Holmusk, Intra-Cellular Therapies, Jamjoom Pharma, Janssen/J&J, Karuna, LB Pharma, Lundbeck, MedinCell, MedLink Global, Merck, MindPax, Mitsubishi Tanabe Pharmaceuticals, MapLight, Mylan, Neumora Therapeutics, Neuraxpharm, Neurocrine, Neurelis, Neurosterix, NeuShen, Neusignal Therapeutics, Newron, Noven, Novo Nordisk, Orion Pharma, Otsuka, PPD Biotech, Recognify Life Science, Recordati, Relmada, Response Pharmaceutical, Reviva, Rovi, Saladax, Sanofi, Seqirus, Servier, Sumitomo Pharma America, Sunovion, Sun Pharma, Supernus, Tabuk, Takeda, Teva, Terran, Tolmar, Vertex, Viatris, and Xenon Pharmaceuticals; provided expert testimony for Janssen, Lundbeck, Neurocrine, and Otsuka; served on a data safety monitoring board for Compass Pathways, Intra-Cellular Therapies, Relmada, Reviva, and Rovi; received grant support from Boehringer-Ingelheim, Janssen, and Takeda; received royalties from UpToDate; and is also a stock option or stock holder of Cardio Diagnostics, Küleon Biosciences, LB Pharmaceuticals, MedLink Global, MindPax, Quantic, and Terran.

RJ has been a consultant for AbbVie, Acadia, Adamas, Alfasigma, Alkermes, Almatica, Axsome, Biogen, Boehringer Ingelheim, Cingulate Therapeutics, Corium, Eisai, Evidera, Impel, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Osmotica, Otsuka, Pamlab, Pfizer, Sage Therapeutics, Shire, Sunovion, Supernus, Takeda, Teva, Transcend Therapeutics, and Viatris; received speaker/promotional honoraria from AbbVie, Alkermes, Almatica, Axsome, Corium, Eisai, Intra-Cellular Therapies, Ironshore Pharmaceuticals, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Otsuka, Pamlab, Pfizer, Shire, Sunovion, Takeda, Tris Pharmaceuticals, and Viatris; served on an advisory board for Adamas, Alkermes, Corium, Eisai, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Otsuka, Pamlab, Pfizer, Sage Therapeutics, Shire, Sunovion, Supernus, Takeda, and Teva; and received research funding from AbbVie, Lilly, Lundbeck, Otsuka, Pfizer, Shire, and Takeda.

CC has been a consultant or on an advisory board for or has received grant or research support from Acadia, Axsome, Harmony, Neurocrine, and Teva; has served as a consultant for AbbVie, Alkermes, Arcadia, Axsome, Biogen, Boehringer Ingelheim, Corium, Intra-Cellular, Janssen, Karuna, Lundbeck, MedinCell, Moderna, Neurocrine, Noven, Otsuka, Sage, Sumitomo, Supernus, and Teva; has received payment or honoraria for educational activities from AbbVie, Acadia, Alkermes, Axsome, Bristol Myers Squibb, Corium, Intra-Cellular, Janssen, Karuna, Lundbeck, Merck, Neurocrine, Noven, Otsuka, Sumitomo, and Teva; has received support for attending meetings/travel from AbbVie, Acadia, Alkermes, Axsome, Bristol Myers Squibb, Corium, Intra-Cellular, Janssen, Karuna, Lundbeck, Merck, Neurocrine, Noven, Otsuka, Sumitomo, and Teva; and has served on an advisory or data safety monitoring board for AbbVie, Acadia, Alkermes, Axsome, Biogen, Bristol Myers Squibb, Corium, Idorsia, Intra-Cellular, Janssen, Karuna, Lundbeck, Moderna, Neurocrine, Noven, Otsuka, Sage, Sumitomo, and Teva.

HEO has been a consultant for AbbVie, Alkermes, Axsome, Biogen, Bristol Myers Squibb, Intra-Cellular Therapies, Janssen, Karuna, Neurocrine, Otsuka, Sage Therapeutics, and Sunovion; is on the speakers' bureau and has received honoraria from Alkermes, Bristol Myers Squibb, Intra-Cellular Therapies, Johnson & Johnson, Luye Pharma, Lundbeck, Neurocrine, and Teva; receives no royalties; and holds no stock options.

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