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 (proxy for relapse) acute care events 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

Data Source

- Administrative claims data from October 18, 2020, to December 31, 2024, obtained from the Komodo Healthcare Map were analyzed retrospectively
- The Komodo Healthcare Map is a deidentified US-based database with health membership information for ~150 million patients covered by a commercial (66%), Medicaid (27%), or Medicare Advantage (7%) plan

Patients and Study Design

Inclusion Criteria

- Age ≥18 years with ≥1 pharmacy or medical claim for OLZ/SAM or a comparator oral SGA (aripiprazole, brexpiprazole, cariprazine, lumateperone, lurasidone, olanzapine, or risperidone) between October 18, 2021, and December 31, 2023
- ≥12 months of continuous enrollment with medical and pharmacy benefits before and after the index date (date of first medical or pharmacy claim for OLZ/SAM or a comparator SGA)
  - –OLZ/SAM claims were prioritized over comparator SGA claims
- ≥1 medical claim for a diagnosis of schizophrenia during the baseline or follow-up period
- Enrollment in Medicaid insurance as of the index date

Exclusion Criteria

- Any pharmacy or medical claim for the index medication during the baseline period
- Any pharmacy or medical claim for both OLZ/SAM and a comparator SGA on the same index date

Statistics

- Inverse probability treatment weighting was used to balance cohorts on key demographic/clinical covariates

RESULTS

- A total of 45,566 patients with schizophrenia were included
- After weighting, all treatment cohorts were balanced on baseline demographic, clinical, and healthcare resource utilization variables (**Table 1**; the full table, including baseline geographic region, comorbidity profile, medication use, and healthcare resource utilization [all-cause, mental health–related, and schizophrenia-related events], is available via the QR code)
- 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 1**)
- 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 1**)
- Patients initiating OLZ/SAM vs comparator 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**)
- 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 3**)

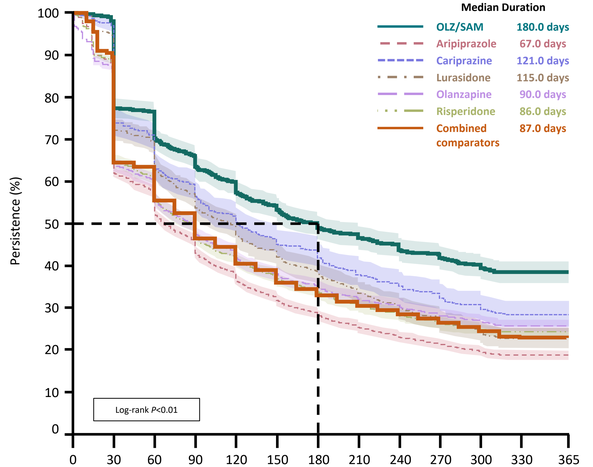
RESULTS

Table 1. Weighted Baseline Patient Demographics[a,b]

	OLZ/SAM (n=1244)	Aripiprazole (n=11,995)	Cariprazine (n=1650)	Lurasidone (n=2030)	Olanzapine (n=14,630)	Risperidone (n=13,173)	Combined Comparators[c] (n=44,322)
Age group, n (%)							
18–24 years	157 (12.6)	1494 (12.5)	223 (13.5)	254 (12.5)	1843 (12.6)	1673 (12.7)	5590 (12.6)
25–34 years	412 (33.1)	3961 (33.0)	554 (33.6)	679 (33.4)	4755 (32.5)	4348 (33.0)	14,647 (33.1)
35–44 years	346 (27.8)	3370 (28.1)	444 (26.9)	570 (28.1)	4152 (28.4)	3657 (27.8)	12,362 (27.9)
45–54 years	175 (14.1)	1687 (14.1)	228 (13.8)	276 (13.6)	2047 (14.0)	1850 (14.0)	6232 (14.1)
55–64 years	145 (11.7)	1369 (11.4)	185 (11.2)	235 (11.6)	1641 (11.2)	1492 (11.3)	5011 (11.3)
≥65 years	9 (0.7)	114 (1.0)	15 (0.9)	16 (0.8)	192 (1.3)	152 (1.2)	480 (1.1)
Female, n (%)	590 (47.4)	5717 (47.7)	794 (48.1)	981 (48.3)	6945 (47.5)	6200 (47.1)	21,066 (47.5)

[a]The full table, including baseline geographic region, Charlson Comorbidity Index category, comorbid conditions, medication use, and healthcare resource utilization (all-cause, mental health–related, and schizophrenia-related events), is available via the QR code. [b]Comparisons to brexpiprazole (n=421) and lumateperone (n=423) were not assessed as separate cohorts due to the relatively low numbers of patients treated with these medications vs OLZ/SAM. [c]Includes the brexpiprazole and lumateperone cohorts.
OLZ/SAM, combination olanzapine and samidorphan.

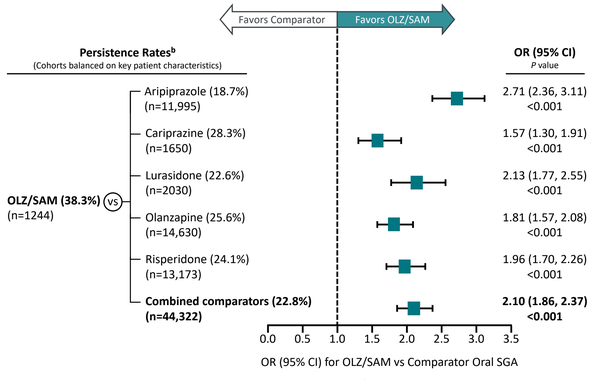
Figure 1. Kaplan-Meier Curves of Probability of Persistence[a] and Duration of Persistence



	OLZ/SAM (n=1244)	Aripiprazole (n=11,995)	Cariprazine (n=1650)	Lurasidone (n=2030)	Olanzapine (n=14,630)	Risperidone (n=13,173)	Combined Comparators[b] (n=44,322)
Persistence,[c] 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)*	146.0 (136.2)*

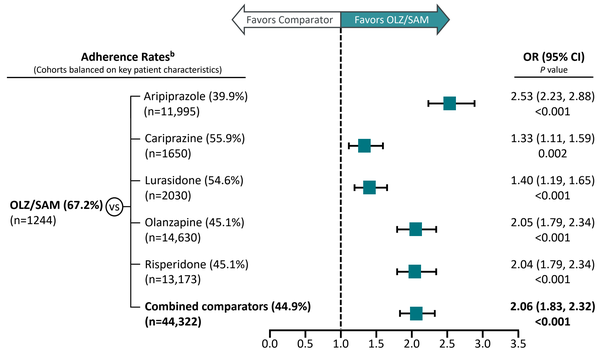
*P<0.01. [a]Duration of persistence measured as the number of days from the index date to the discontinuation date (for patients who discontinued) or from the index date to the end of the follow-up period (for patients who did not discontinue). [b]Includes the brexpiprazole and lumateperone cohorts. [c]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 [79.9]; n=423), data are not compared as separate cohorts with OLZ/SAM.
OLZ/SAM, combination olanzapine and samidorphan.

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



[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 as separate cohorts with OLZ/SAM; however, both were included in the combined comparators cohort. OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio; SGA, second-generation antipsychotic.

Figure 3. Adherence[a] Rates During 12-Month Follow-up: OLZ/SAM vs Comparator Oral SGAs



[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 as separate cohorts with OLZ/SAM; however, both were included in the combined comparators cohort. OLZ/SAM, combination olanzapine and samidorphan; MPR, medication possession ratio; 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 as separate cohorts with OLZ/SAM. [b]Based on odds ratios for persistence and adherence; corresponds to a 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]

ACKNOWLEDGMENTS

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RESULTS

Table 1. Weighted Baseline Patient Demographics, Clinical Characteristics, Medication Use, and Healthcare Resource Utilization[a]

	OLZ/SAM (n=1244)	Aripiprazole (n=11,995)	Cariprazine (n=1650)	Lurasidone (n=2030)	Olanzapine (n=14,630)	Risperidone (n=13,173)	Combined Comparators[b] (n=44,322)
Age group, n (%)							
18–24 years	157 (12.6)	1494 (12.5)	223 (13.5)	254 (12.5)	1843 (12.6)	1673 (12.7)	5590 (12.6)
25–34 years	412 (33.1)	3961 (33.0)	554 (33.6)	679 (33.4)	4755 (32.5)	4348 (33.0)	14,647 (33.1)
35–44 years	346 (27.8)	3370 (28.1)	444 (26.9)	570 (28.1)	4152 (28.4)	3657 (27.8)	12,362 (27.9)
45–54 years	175 (14.1)	1687 (14.1)	228 (13.8)	276 (13.6)	2047 (14.0)	1850 (14.0)	6232 (14.1)
55–64 years	145 (11.7)	1369 (11.4)	185 (11.2)	235 (11.6)	1641 (11.2)	1492 (11.3)	5011 (11.3)
≥65 years	9 (0.7)	114 (1.0)	15 (0.9)	16 (0.8)	192 (1.3)	152 (1.2)	480 (1.1)
Female, n (%)	590 (47.4)	5717 (47.7)	794 (48.1)	981 (48.3)	6945 (47.5)	6200 (47.1)	21,066 (47.5)
Region, n (%)							
West	455 (36.6)	4445 (37.1)	602 (36.5)	744 (36.7)	5521 (37.7)	5007 (38.0)	16,310 (36.8)
South	338 (27.2)	3242 (27.0)	444 (26.9)	566 (27.9)	3972 (27.1)	3507 (26.6)	12,027 (27.1)
Midwest	275 (22.1)	2664 (22.2)	372 (22.5)	452 (22.3)	3168 (21.7)	2857 (21.7)	9798 (22.1)
Northeast	176 (14.1)	1641 (13.7)	232 (14.1)	267 (13.2)	1967 (13.4)	1798 (13.6)	6178 (13.9)
Other	0	3 (0.02)	1 (0.03)	1 (0.05)	2 (0.01)	3 (0.03)	9 (0.02)
Charlson Comorbidity Index category, n (%)							
0	825 (66.3)	7979 (66.5)	1103 (66.8)	1341 (66.1)	9699 (66.3)	8775 (66.6)	29,412 (66.4)
1–2	318 (25.6)	3054 (25.5)	425 (25.8)	522 (25.7)	3751 (25.6)	3364 (25.5)	11,334 (25.6)
3–4	77 (6.2)	682 (5.7)	93 (5.6)	115 (5.7)	781 (5.3)	760 (5.8)	2506 (5.7)
≥5	24 (1.9)	280 (2.3)	29 (1.8)	52 (2.6)	399 (2.7)	274 (2.1)	1071 (2.4)
Comorbid conditions, n (%)							
Anxiety disorder	636 (51.1)	6131 (51.1)	884 (53.6)	1046 (51.5)	7547 (51.6)	6793 (51.6)	22,697 (51.2)
Obesity	513 (41.2)	4978 (41.5)	665 (40.3)	834 (41.1)	6092 (41.6)	5453 (41.4)	18,324 (41.3)
Any substance use disorder	497 (40.0)	4750 (39.6)	670 (40.6)	821 (40.4)	5751 (39.3)	5173 (39.3)	17,647 (39.8)
Major depressive disorder	448 (36.0)	4255 (35.5)	603 (36.5)	731 (36.0)	5230 (35.7)	4735 (35.9)	15,925 (35.9)
Hypertension	428 (34.4)	4086 (34.1)	554 (33.6)	694 (34.2)	5031 (34.4)	4475 (34.0)	15,192 (34.3)
Hyperlipidemia	403 (32.4)	3850 (32.1)	511 (31.0)	638 (31.4)	4680 (32.0)	4224 (32.1)	14,307 (32.3)
Posttraumatic stress disorder	249 (20.0)	2434 (20.3)	355 (21.5)	435 (21.4)	3043 (20.8)	2738 (20.8)	8958 (20.2)
Type 2 diabetes	231 (18.6)	2201 (18.3)	321 (19.5)	379 (18.7)	2719 (18.6)	2423 (18.4)	8207 (18.5)
Alcohol use disorder	230 (18.5)	2201 (18.3)	310 (18.8)	368 (18.1)	2640 (18.0)	2363 (17.9)	8155 (18.4)
Intentional self-inflicted injury	151 (12.1)	1442 (12.0)	208 (12.6)	247 (12.2)	1749 (12.0)	1596 (12.1)	5362 (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)	26,103 (58.9)
Behavioral health medication	1122 (90.2)	10,838 (90.4)	1499 (90.8)	1835 (90.4)	13,236 (90.5)	11,920 (90.5)	40,008 (90.3)
Any other medication	723 (58.1)	6984 (58.2)	955 (57.9)	1165 (57.4)	8562 (58.5)	7728 (58.7)	25,801 (58.2)
All-cause events, n (%)							
Inpatient admissions	494 (39.7)	4692 (39.1)	670 (40.6)	805 (39.7)	5745 (39.3)	5132 (39.0)	17,509 (39.5)
ED visits	785 (63.1)	7509 (62.6)	1059 (64.2)	1292 (63.7)	9124 (62.4)	8189 (62.2)	27,876 (62.9)
Outpatient visits	1205 (96.9)	11,635 (97.0)	1605 (97.3)	1969 (97.0)	14,187 (97.0)	12,769 (96.9)	42,947 (96.9)
Mental health–related events, n (%)							
Inpatient admissions	447 (35.9)	4249 (35.4)	604 (36.6)	736 (36.3)	5201 (35.6)	4660 (35.4)	15,853 (35.8)
ED visits	574 (46.1)	5484 (45.7)	786 (47.6)	945 (46.6)	6702 (45.8)	5993 (45.5)	20,387 (46.0)
Outpatient visits	1122 (90.2)	10,872 (90.6)	1504 (91.1)	1839 (90.6)	13,258 (90.6)	11,924 (90.5)	40,033 (90.3)
Schizophrenia-related events, n (%)							
Inpatient admissions	336 (27.0)	3196 (26.6)	456 (27.6)	558 (27.5)	3908 (26.7)	3507 (26.6)	11,917 (26.9)
ED visits	356 (28.6)	3426 (28.6)	490 (29.7)	598 (29.5)	4196 (28.7)	3783 (28.7)	12,689 (28.6)
Outpatient visits	953 (76.6)	9261 (77.2)	1291 (78.2)	1557 (76.7)	11,269 (77.0)	10,166 (77.2)	34,029 (76.8)

[a]Comparisons to brexpiprazole (n=421) and lumateperone (n=423) were not assessed as separate cohorts due to the relatively low numbers of patients treated with these medications vs OLZ/SAM. [b]Includes the brexpiprazole and lumateperone cohorts.
ED, emergency department; OLZ/SAM, combination olanzapine and samidorphan.

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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, Helus Pharma, Incannex Healthcare, Intra-Cellular Therapies, J&J Innovative Medicine, Jazz Pharma, Knight Therapeutics, Kuvatris Therapeutics, Kye Pharmaceuticals, LivaNova, Lundbeck, Luye Pharma, 4M Therapeutics, MapLight Therapeutics, Mentavi, Neumora, Neurocrine Biosciences, Noven, Otsuka, 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, 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, Sensorium Therapeutics, and Transneural Therapeutics.

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