Real-World Comparison of Olanzapine/Samidorphan vs Olanzapine: An Assessment of Treatment Patterns and Acute Care Events Among Patients With Schizophrenia

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BACKGROUND

- Olanzapine/samidorphan (OLZ/SAM) provides the antipsychotic efficacy of olanzapine while mitigating olanzapine-associated weight gain in patients with schizophrenia or bipolar I disorder[1,2]
- OLZ/SAM has also maintained symptom control and had a long-term safety profile over 4 years with small changes in body weight and minimal changes in lipid and glycemic parameters over extended duration[3]
- Previous real-world analyses have shown significant decreases in acute care events, as measured by inpatient (IP) admissions or emergency department (ED) visits, in the 6 and 12 months following OLZ/SAM initiation[4-6]
- To our knowledge, there have been no real-world studies examining such real-world effectiveness benefits for OLZ/SAM vs olanzapine

OBJECTIVE

- To assess and compare treatment patterns and acute care events in adult Medicaid-insured patients with schizophrenia initiating OLZ/SAM vs olanzapine

METHODS

Data Source

- Administrative claims data from October 18, 2020, to December 31, 2023, for Medicaid-insured patients obtained from the Komodo Healthcare Map were analyzed retrospectively
  - The Komodo Healthcare Map is a fully deidentified US-based database with health plan membership information for ~150 million patients, 27% of whom are covered by Medicaid

Patients and Study Design

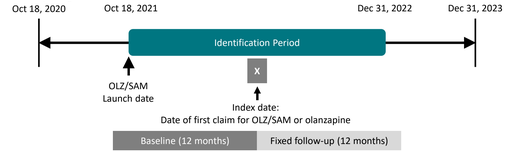
Inclusion Criteria

- Age ≥18 years with ≥1 pharmacy or medical claim for OLZ/SAM or olanzapine during the identification period
- ≥12 months of continuous enrollment with medical and pharmacy benefits before (baseline period) and after (fixed follow-up period) the index date (date of first medical or pharmacy claim for OLZ/SAM or olanzapine)
  - Selection criteria for determining index medication was hierarchical; OLZ/SAM claims were prioritized over olanzapine claims
- ≥1 medical claim for 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 olanzapine on the same index date

Figure 1. Study Design



OLZ/SAM, olanzapine combined with samidorphan.

Outcomes

- Demographics and baseline clinical characteristics
- Treatment patterns
  - Adherence: medication possession ratio (MPR), 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
  - Persistence: the number of days from the index date to the discontinuation date (for patients who discontinue) or from the index date to the end of the follow-up period (for patients who do not discontinue)
  - Discontinuation: a minimum 45-day gap in index medication therapy
- Acute care events in a 12-month follow-up period in all-cause, mental health–related, and schizophrenia-related categories, IP admissions, ED visits, times to first IP admission, and numbers of days hospitalized per patient
  - Relapse was defined as ≥1 schizophrenia-related IP admission or ED visit

Statistics

- Propensity score matching was conducted to achieve balanced OLZ/SAM and olanzapine cohorts, with standardized differences of <10% retained between cohorts to ensure sufficient balance
  - Patients were matched 1:1 on key demographic/clinical covariates: age, sex, baseline comorbidity profile, antipsychotic use, behavioral health and other medication use, and baseline acute care events (all cause, mental health related, disease related)
- Comparisons between matched cohorts were modeled using a generalized linear model—a logistic model with a logit link for dichotomous outcomes—and Poisson models with log link for counts and non-normally distributed continuous outcomes
  - In each model, the outcome was the dependent variable, and the cohorts were the only independent variable
  - Dichotomous outcomes were presented as odds ratios, with *P* values and 95% CIs
  - Counts and non-normally distributed continuous outcomes were presented as count ratios of the mean values, with *P* values and 95% CIs
- Kaplan-Meier analysis was used to evaluate persistence between OLZ/SAM and olanzapine

RESULTS

- After applying eligibility criteria, 16,523 patients with schizophrenia (OLZ/SAM, n=807; olanzapine, n=15,716) were included

Table 1. Unmatched Baseline Patient Demographics

Characteristics	OLZ/SAM (n=807)	Olanzapine (n=15,716)
Age, mean (SD), years	37.3 (12.0)	37.8 (12.9)
Sex, n (%)		
Female	386 (47.8)	6059 (38.6)
Male	417 (51.7)	9621 (61.2)
Unknown	4 (0.5)	36 (0.2)
Region, n (%)		
Northeast	106 (13.1)	3037 (19.3)
Midwest	168 (20.8)	2965 (18.9)
South	229 (28.4)	4548 (28.9)
West	304 (37.7)	5166 (32.9)

OLZ/SAM, combination olanzapine and samidorphan.

Table 2. Unmatched Baseline Clinical Characteristics

Characteristics	OLZ/SAM (n=807)	Olanzapine (n=15,716)
Charlson comorbidity score, mean (SD), years	0.6 (1.1)	0.8 (1.5)
Comorbid conditions, n (%)		
Anxiety disorder	419 (51.9)	8701 (55.4)
Any substance use disorder	323 (40.0)	9486 (60.4)
Obesity	322 (39.9)	3287 (20.9)
Major depressive disorder	307 (38.0)	7194 (45.8)
Hypertension	264 (32.7)	5489 (34.9)
Hyperlipidemia	262 (32.5)	3513 (22.4)
Posttraumatic stress disorder	158 (19.6)	3242 (20.6)
Type 2 diabetes	142 (17.6)	2278 (14.5)
Alcohol use disorder	141 (17.5)	4102 (26.1)
Intentional self-inflicted injury	91 (11.3)	2531 (16.1)
Antipsychotic use during baseline period, n (%)		
Any second-generation oral[a]	766 (94.9)	8598 (54.7)
Any first-generation oral	178 (22.1)	3874 (24.7)
Any second-generation LAI	168 (20.8)	2079 (13.2)
Any first-generation LAI	40 (5.0)	640 (4.1)
None	17 (2.1)	5246 (33.4)
Other medications taken during baseline period, n (%)		
Antidepressant	565 (70.0)	8088 (51.5)
Mood stabilizer	457 (56.6)	6350 (40.4)
Anxiolytic	397 (49.2)	6591 (41.9)
Antihypertensive	389 (48.2)	5360 (34.1)
Metformin	145 (18.0)	1202 (7.7)
Patients with type 2 diabetes	89 (62.7)	991 (43.5)

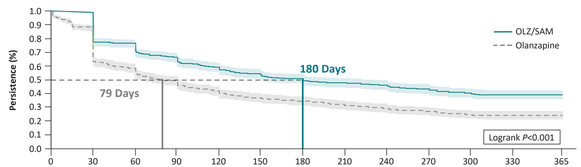
[a]Olanzapine was taken by 560 (69.4%) patients in the OLZ/SAM group during the baseline period.
LAI, long-acting injectable; OLZ/SAM, combination olanzapine and samidorphan.

- After propensity score matching to balance differences between cohorts, 1614 patients with schizophrenia (OLZ/SAM, n=807; olanzapine, n=807) were included in analyses; key covariates were well-balanced (standardized mean differences <10%) between the two cohorts

Treatment Patterns

- At 12 months, 39.0% of patients were persistent on OLZ/SAM vs 24.2% on olanzapine
- Median days persistent: 180 days vs 79 days for OLZ/SAM vs olanzapine

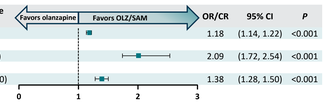
Figure 2. Kaplan-Meier Curves of Probability of Persistence



OLZ/SAM, combination olanzapine and samidorphan.

- OLZ/SAM was associated with significantly higher adherence and longer persistence over 12 months vs olanzapine
- Odds of discontinuation were 50% lower with OLZ/SAM vs olanzapine (61.0% vs 75.8%, OR [95% CI]: 0.50 [0.40, 0.61], *P*<0.001)

Figure 3. Treatment Patterns[a]



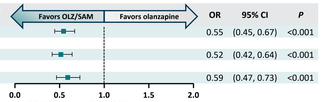
Acute Care Event Type	OLZ/SAM (n=807)	Olanzapine (n=807)	OR/CR	95% CI	P
Adherence, MPR, mean (SD)	0.9 (0.2)	0.8 (0.3)	1.18	(1.14, 1.22)	<0.001
Adherence, MPR ≥0.80, n (%)	509 (63.1)	363 (45.0)	2.09	(1.72, 2.54)	<0.001
Persistence, days, mean (SD)	202.9 (144.3)	146.8 (140.0)	1.38	(1.28, 1.50)	<0.001

[a]Adherence and persistence are presented as CRs, MPR ≥0.80 as an OR.
CR, count ratio; MPR, medication possession ratio; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: IP Admissions

- OLZ/SAM was associated with significantly lower likelihood of ≥1 all-cause, mental health–related, or schizophrenia-related IP admission

Figure 4. Percent of Patients With ≥1 IP Admission



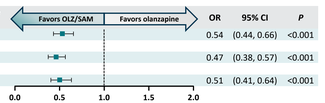
Acute Care Event Type	OLZ/SAM (n=807)	Olanzapine (n=807)	OR	95% CI	P
All cause, n (%)	257 (31.9)	371 (46.0)	0.55	(0.45, 0.67)	<0.001
Mental health related, n (%)	227 (28.1)	347 (43.0)	0.52	(0.42, 0.64)	<0.001
Schizophrenia related, n (%)	195 (24.2)	284 (35.2)	0.59	(0.47, 0.73)	<0.001

IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: ED Visits

- OLZ/SAM was associated with significantly lower likelihood of ≥1 all-cause, mental health–related, or schizophrenia-related ED visit

Figure 5. Percent of Patients With ≥1 ED Visit



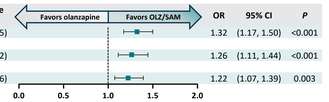
Acute Care Event Type	OLZ/SAM (n=807)	Olanzapine (n=807)	OR	95% CI	P
All cause, n (%)	433 (53.7)	551 (68.3)	0.54	(0.44, 0.66)	<0.001
Mental health related, n (%)	263 (32.6)	411 (50.9)	0.47	(0.38, 0.57)	<0.001
Schizophrenia related, n (%)	173 (21.4)	281 (34.8)	0.51	(0.41, 0.64)	<0.001

ED, emergency department; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: Number of Days to First IP Admission

- Across all-cause, mental health–related, and schizophrenia-related events, mean numbers of days to first IP admission were significantly longer in patients initiating OLZ/SAM vs olanzapine

Figure 6. Numbers of Days to First IP Admission



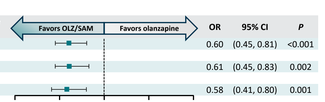
Acute Care Event Type	OLZ/SAM (n=807)	Olanzapine (n=807)	OR	95% CI	P
All cause, mean (SD), days	155.5 (112.3)	117.4 (107.5)	1.32	(1.17, 1.50)	<0.001
Mental health related, mean (SD), days	151.7 (110.2)	120.1 (108.2)	1.26	(1.11, 1.44)	<0.001
Schizophrenia related, mean (SD), days	161.9 (110.0)	132.7 (109.6)	1.22	(1.07, 1.39)	0.003

IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: Number of Days Hospitalized

- Across all-cause, mental health–related, and schizophrenia-related events, mean numbers of days hospitalized per patient were significantly lower in patients initiating OLZ/SAM vs olanzapine

Figure 7. Numbers of Days Hospitalized Per Patient



Acute Care Event Type	OLZ/SAM (n=807)	Olanzapine (n=807)	OR	95% CI	P
All cause, mean (SD), days	8.6 (29.9)	14.3 (36.1)	0.60	(0.45, 0.81)	<0.001
Mental health related, mean (SD), days	8.2 (29.3)	13.4 (34.3)	0.61	(0.45, 0.83)	0.002
Schizophrenia related, mean (SD), days	6.4 (24.6)	11.0 (31.8)	0.58	(0.41, 0.80)	0.001

OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Clinical Context: A cohort of patients with schizophrenia initiated on OLZ/SAM vs olanzapine demonstrated

109% higher odds of **being adherent** (MPR ≥0.80)
OR (95% CI): 2.09 (1.72, 2.54); *P*<0.001

50% lower odds of **discontinuation**
OR (95% CI): 0.50 (0.40, 0.61); *P*<0.001

69% higher odds of **being relapse-free**[a]
OR (95% CI): 0.59 (0.47, 0.73); *P*<0.001

[a]Calculated based on OR of schizophrenia-related IP admissions (used as a proxy for relapse); schizophrenia-related ED visits were not included.
ED, emergency department; IP, inpatient; MPR, medication possession ratio; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

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 are 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 olanzapine 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 of multiplicity was performed for the statistical tests used in these analyses

CONCLUSIONS

- Initiating OLZ/SAM treatment resulted in
  - Significantly higher adherence, longer persistence, and lower likelihood of discontinuation vs olanzapine
  - Significantly lower likelihood of schizophrenia-related (relapse), mental health–related, and all-cause acute care events vs olanzapine
- OLZ/SAM treatment offers meaningful benefits over olanzapine, as observed by favorable treatment patterns and lower likelihood of relapse and related acute care events

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DISCLOSURES

AJC has been a consultant to or on an advisory board for AbbVie, Acadia, Alfasigma, Alkermes, Anavex Life Sciences, Autobahn Therapeutics, Axsome, Biogen, Biohaven, Boehringer Ingelheim, Bril Biosciences, Bristol Myers Squibb, Cerevel, Corium, Delpor, Evolution Research Group, Intra-Cellular Therapies, J&J Innovative Medicine, Jazz Pharma, Karuna, LivaNova, Lundbeck, Luye Pharma, 4M Therapeutics, MapLight Therapeutics, MedAvante-ProPhase, Mentavi, Neumora, Neurocrine, Neuroscience Education Institute, NeuroSigma, Noven, Otsuka, PaxMedica, Relmada, Sage Therapeutics, Supernus, Teva, Thynk, Tris Pharma, Vanda Pharmaceuticals, and VistaGen; is on the speakers' bureau for AbbVie, Alfasigma, Alkermes, Axsome, Bristol Myers Squibb, Corium, Intra-Cellular Therapies, J&J, Lundbeck, Neurocrine, Noven, Otsuka, Supernus, Teva, Tris Pharma, and Vanda Pharmaceuticals; is on a data safety monitoring board for Alar Pharma, COMPASS Pathways, Freedom Biosciences, and Pain Therapeutics; holds stock options from 4M Therapeutics; and receives no royalties.
HRP and **MJD** are or were employees of Alkermes, Inc., and may own stock/options in the company.
AGH is or was an employee of Optum, Inc., a health services innovation company that received funding from Alkermes, Inc., to conduct this study and analyze the data used for this publication.
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.
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 Vitrix; 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 Vitrix; 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.

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Key Contributors

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the poster; gave final approval of the version to be presented; and agree to be accountable for all aspects of the work.

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