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

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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 (BD-I)[1,2]
- In a 4-year open-label study, OLZ/SAM also maintained symptom control with small changes in body weight and minimal changes in lipid and glycemic parameters over 4 years of treatment[3]
- Previous real-world analyses have shown significant reductions 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 the effectiveness of OLZ/SAM vs olanzapine

OBJECTIVE

- To assess and compare treatment patterns and acute care events in adult Medicaid-insured patients with schizophrenia or BD-I 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 (approximately 60% of the full Medicaid population)[7]

Patients and Study Design (Figure 1)

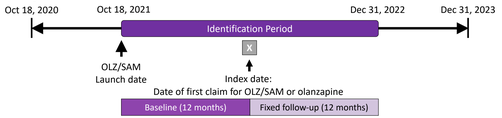
Inclusion Criteria

- 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 (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 or BD-I during the baseline or follow-up period; patients with medical claims for both diagnoses were assigned to the schizophrenia cohort
- 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



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 discontinued) or from the index date to the end of the follow-up period (for patients who did 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, and numbers of days to first IP admission
  - Relapse was defined as ≥1 disease-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% preserved between cohorts to ensure sufficient balance
  - Patients were matched 1:1 on key demographic/clinical covariates: age group, 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 (ORs), with *P* values and 95% CIs
  - Counts and non-normally distributed continuous outcomes were presented as count ratios (CRs) of the mean values, with *P* values and 95% CIs
- Kaplan-Meier analysis was used to evaluate persistence between OLZ/SAM and olanzapine
- No adjustments were made for multiplicity

RESULTS: Schizophrenia

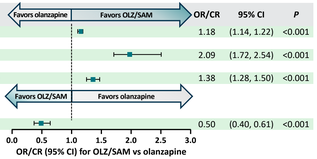
- After propensity score matching to balance differences between cohorts, 1614 patients with schizophrenia (OLZ/SAM, n=807; olanzapine, n=807) were included; key covariates were well balanced (standardized mean differences <10%) between the two cohorts

Treatment Patterns

- OLZ/SAM was associated with significantly higher adherence, longer persistence, and lower odds of discontinuation over 12 months vs olanzapine (**Figure 2**)
  - **Adherence**: Odds of adherence (MPR ≥0.80) were 109% higher with OLZ/SAM vs olanzapine (63.1% vs 45.0%, respectively; OR [95% CI]: 2.09 [1.72, 2.54]; *P*<0.001)
  - **Persistence**: Higher rates of persistence and longer duration of persistence were observed with OLZ/SAM vs olanzapine
    - Based on Kaplan-Meier curve analysis (not shown), at 12 months, 39.0% of patients were persistent on OLZ/SAM vs 24.2% on olanzapine; median days persistent were 180 days vs 79 days for OLZ/SAM vs olanzapine, respectively
    - Mean (SD) numbers of days persistent were 202.9 days (144.3) for the OLZ/SAM cohort and 146.8 days (140.0) for the olanzapine cohort (CR [95% CI]: 1.38 [1.28, 1.50]; *P*<0.001), thus 38% higher with OLZ/SAM than with olanzapine
  - **Discontinuation:** Odds of discontinuation were 50% lower with OLZ/SAM vs olanzapine (61.0% vs 75.8%, respectively; OR [95% CI]: 0.50 [0.40, 0.61]; *P*<0.001)

Figure 2. Treatment Patterns[a]

Treatment Patterns	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
Discontinuation, n (%)	492 (61.0)	612 (75.8)	0.50	(0.40, 0.61)	<0.001



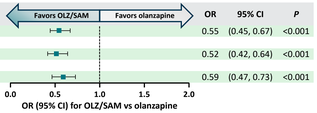
[a]Mean adherence and persistence are presented as CRs and MPR ≥0.80 and discontinuation as ORs.
CR, count ratio; MPR, medication possession ratio; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events

- OLZ/SAM was associated with significantly lower likelihood of ≥1 all-cause, mental health–related, or schizophrenia-related IP admission (**Figure 3**) or ED visit (**Figure 4**), and with a significantly longer number of days to first IP admission (**Figure 5**) in patients with schizophrenia

Figure 3. Percentages of Patients With ≥1 IP Admission

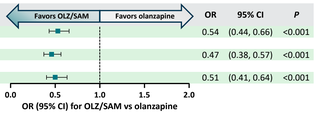
Acute Care Event Types	OLZ/SAM (n=807)	Olanzapine (n=807)	OR	95% CI	*P*
All cause, n (%)	257 (31.9)	371 (46.0)	0.55	(0.45, 0.67)	<0.001
Mental health related, n (%)	227 (28.1)	347 (43.0)	0.52	(0.42, 0.64)	<0.001
Schizophrenia related, n (%)	195 (24.2)	284 (35.2)	0.59	(0.47, 0.73)	<0.001



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

Figure 4. Percentages of Patients With ≥1 ED Visit

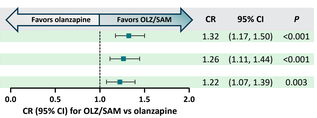
Acute Care Event Types	OLZ/SAM (n=807)	Olanzapine (n=807)	OR	95% CI	*P*
All cause, n (%)	433 (53.7)	551 (68.3)	0.54	(0.44, 0.66)	<0.001
Mental health related, n (%)	263 (32.6)	411 (50.9)	0.47	(0.38, 0.57)	<0.001
Schizophrenia related, n (%)	173 (21.4)	281 (34.8)	0.51	(0.41, 0.64)	<0.001



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

Figure 5. Numbers of Days to First IP Admission

Acute Care Event Types	OLZ/SAM (n=807)	Olanzapine (n=807)	CR	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



CR, count ratio; IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan.

RESULTS: BD-I

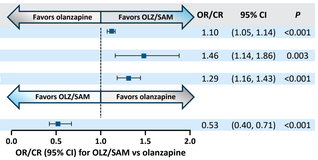
- After propensity score matching to balance differences between cohorts, 1008 patients with BD-I (OLZ/SAM, n=504; olanzapine, n=504) were included; key covariates were well balanced (standardized mean differences <10%) between the two cohorts

Treatment Patterns

- OLZ/SAM was associated with significantly higher adherence, longer persistence, and lower odds of discontinuation over 12 months vs olanzapine (**Figure 6**)
  - **Adherence:** Odds of adherence (MPR ≥0.80) were 46% higher with OLZ/SAM vs olanzapine (57.5% vs 48.2%, respectively; OR [95% CI]: 1.46 [1.14, 1.86]; *P*=0.003)
  - **Persistence:** Higher rates of persistence and longer duration of persistence were observed with OLZ/SAM vs olanzapine
    - Based on Kaplan-Meier curve analysis (not shown), at 12 months, 33.1% of patients were persistent on OLZ/SAM vs 20.8% on olanzapine; median days persistent were 150 days vs 90 days for OLZ/SAM vs olanzapine, respectively
    - Mean (SD) numbers of days persistent were 185.3 days (142.1) for the OLZ/SAM cohort and 143.6 days (132.4) for the olanzapine cohort (CR [95% CI]: 1.29 [1.16, 1.43; *P*<0.001), thus 29% higher with OLZ/SAM than with olanzapine
  - **Discontinuation:** Odds of discontinuation were almost 50% lower with OLZ/SAM vs olanzapine (66.9% vs 79.2%, respectively; OR [95% CI]: 0.53 [0.40, 0.71]; *P*<0.001)

Figure 6. Treatment Patterns[a]

Treatment Patterns	OLZ/SAM (n=504)	Olanzapine (n=504)	OR/CR	95% CI	*P*
Adherence, MPR, mean (SD)	0.9 (0.2)	0.8 (0.3)	1.10	(1.05, 1.14)	<0.001
Adherence, MPR ≥0.80, n (%)	290 (57.5)	243 (48.2)	1.46	(1.14, 1.86)	0.003
Persistence, days, mean (SD)	185.3 (142.1)	143.6 (132.4)	1.29	(1.16, 1.43)	<0.001
Discontinuation, n (%)	337 (66.9)	399 (79.2)	0.53	(0.40, 0.71)	<0.001



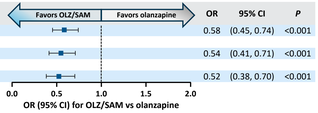
[a]Mean adherence and persistence are presented as CRs and MPR ≥0.80 and discontinuation as ORs.
CR, count ratio; MPR, medication possession ratio; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events

OLZ/SAM was associated with significantly lower likelihood of ≥1 all-cause, mental health–related, or BD-I–related IP admission (**Figure 7**) or ED visit (**Figure 8**), and with a significantly longer number of days to first IP admission (**Figure 9**) in patients with BD-I

Figure 7. Percentages of Patients With ≥1 IP Admission

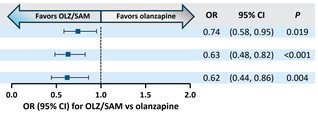
Acute Care Event Types	OLZ/SAM (n=504)	Olanzapine (n=504)	OR	95% CI	*P*
All cause, n (%)	127 (25.2)	186 (36.9)	0.58	(0.45, 0.74)	<0.001
Mental health related, n (%)	107 (21.2)	168 (33.3)	0.54	(0.41, 0.71)	<0.001
BD-I related, n (%)	81 (16.1)	136 (27.0)	0.52	(0.38, 0.70)	<0.001



BD-I, bipolar I disorder; IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Figure 8. Percentages of Patients With ≥1 ED Visit

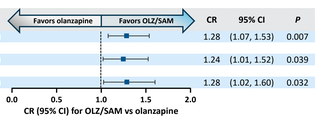
Acute Care Event Types	OLZ/SAM (n=504)	Olanzapine (n=504)	OR	95% CI	*P*
All cause, n (%)	278 (55.2)	314 (62.3)	0.74	(0.58, 0.95)	0.019
Mental health related, n (%)	139 (27.6)	190 (37.7)	0.63	(0.48, 0.82)	<0.001
BD-I related, n (%)	74 (14.7)	110 (21.8)	0.62	(0.44, 0.86)	0.004



BD-I, bipolar I disorder; ED, emergency department; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

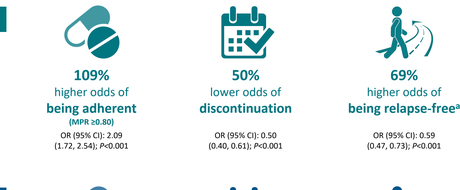
Figure 9. Numbers of Days to First IP Admission

Acute Care Event Types	OLZ/SAM (n=504)	Olanzapine (n=504)	CR	95% CI	*P*
All cause, mean (SD), days	158.4 (110.4)	123.7 (105.0)	1.28	(1.07, 1.53)	0.007
Mental health related, mean (SD), days	147.3 (110.4)	118.8 (103.9)	1.24	(1.01, 1.52)	0.039
BD-I related, mean (SD), days	150.3 (110.4)	117.5 (106.1)	1.28	(1.02, 1.60)	0.032



BD-I, bipolar I disorder; CR, count ratio; IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan.

Clinical context: Cohorts of patients with schizophrenia or BD-I initiated on OLZ/SAM vs olanzapine demonstrated



[a]Calculated based on ORs of disease-related IP admissions (used as a proxy for relapse); disease-related ED visits were not included.
BD-I, bipolar I disorder; 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 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 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

CONCLUSIONS

- Initiating OLZ/SAM vs olanzapine treatment resulted in consistent findings across the schizophrenia and BD-I cohorts
  - Significantly higher adherence, longer persistence, and lower likelihood of discontinuation
  - Significantly lower likelihood of relapse, as assessed by reductions in schizophrenia-related and BD-I–related acute care events
  - Significantly lower likelihood of mental health–related and all-cause acute care events
- 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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[1]Alkermes, Inc., Waltham, MA, USA; [2]Department of Psychiatry, Texas Tech University School of Medicine-Permian Basin, Midland, TX, USA; [3]Optum, Inc., Eden Prairie, MN, USA; [4]Excel Psychiatric Associates, P.A., Huntersville, NC, USA; [5]Atrium Health, Charlotte, NC, USA; [6]Department of Psychiatry, SUNY Upstate Medical University, Syracuse, NY, USA; [7]Neuroscience Education Institute, Lakewood Ranch, FL, USA

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DISCLOSURES

HRP and **MJD** are or were employees of Alkermes, Inc., and may own stock/options in the company.
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.
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, Acadia, Alkermes, Almatica, Axsome, Biogen, Boehringer Ingelheim, Corium, Intra-Cellular Therapies, 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 Therapies, 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 Therapies, Janssen, Karuna, Lundbeck, Merck, Neurocrine, Noven, Otsuka, Sumitomo, Teva, and Tonix; and has served on an advisory or data safety monitoring board for AbbVie, Acadia, Alkermes, Axsome, Biogen, Bristol Myers Squibb, Corium, Idorsia, Intra-Cellular Therapies, Janssen, Karuna, Lundbeck, Moderna, Neurocrine, Noven, Otsuka, Sage, Sumitomo, and Teva.
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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