Real-World Comparison of Olanzapine/Samidorphan vs Olanzapine: An Assessment of Treatment Patterns and Acute Care Events Among Patients With 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]
- 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 an 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 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 de-identified US-based database with health plan membership information for ~150 million patients, 27% of whom are covered by Medicaid

Patients and Study Design

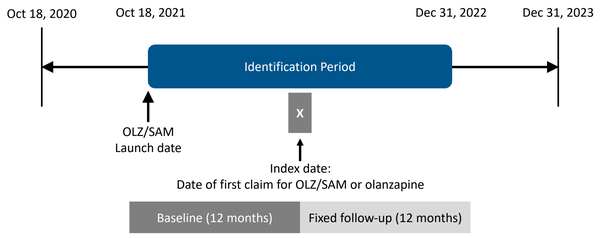
Inclusion Criteria

- 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 BD-I during the baseline or follow-up period
  - Patients with medical claims for both schizophrenia and BD-I were assigned an indication of schizophrenia
- 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 BD-I–related categories including IP admissions, ED visits, times to first IP admission, and numbers of days hospitalized per patient
  - Relapse was defined as ≥1 BD-I–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 period 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 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, 8854 patients with BD-I (OLZ/SAM, n=504; olanzapine, n=8350) were included

Table 1. Unmatched Baseline Patient Demographics

Characteristics	OLZ/SAM (n=504)	Olanzapine (n=8350)
Age, mean (SD), years	36.7 (11.0)	36.3 (11.9)
Sex, n (%)		
Female	353 (70.0)	5085 (60.9)
Male	149 (29.6)	3246 (38.9)
Unknown	2 (0.4)	19 (0.2)
Region, n (%)		
Northeast	78 (15.5)	2069 (24.8)
Midwest	155 (30.8)	1945 (23.3)
South	138 (27.4)	2422 (29.0)
West	133 (26.4)	1913 (22.9)

OLZ/SAM, combination olanzapine and samidorphan.

Table 2. Unmatched Baseline Clinical Characteristics

Characteristics	OLZ/SAM (n=504)	Olanzapine (n=8350)
Charlson comorbidity score, mean (SD), years	0.7 (1.1)	0.7 (1.4)
Comorbid conditions, n (%)		
Anxiety disorder	379 (75.2)	5709 (68.4)
Any substance use disorder	230 (45.6)	4808 (57.6)
Major depressive disorder	227 (45.0)	4237 (50.7)
Obesity	203 (40.3)	1856 (22.2)
Posttraumatic stress disorder	182 (36.1)	2803 (33.6)
Hypertension	139 (27.6)	2388 (28.6)
Hyperlipidemia	135 (26.8)	1617 (19.4)
Alcohol use disorder	102 (20.2)	2101 (25.2)
Type 2 diabetes	81 (16.1)	866 (10.4)
Intentional self-inflicted injury	52 (10.3)	1207 (14.5)
Antipsychotic use during baseline period, n (%)		
Any second-generation oral[a]	451 (89.5)	4332 (51.9)
Any first-generation oral	54 (10.7)	1145 (13.7)
Any second-generation LAI	31 (6.2)	289 (3.5)
Any first-generation LAI	2 (0.4)	27 (0.3)
None	45 (8.9)	3478 (41.7)
Other medication taken during baseline period, n (%)		
Mood stabilizer	387 (76.8)	4594 (55.0)
Antidepressant	382 (75.8)	5175 (62.0)
Anxiolytic	313 (62.1)	4264 (51.1)
Antihypertensive	256 (50.8)	3309 (39.6)
Metformin	84 (16.7)	504 (6.0)
Patients with type 2 diabetes	47 (58.0)	370 (42.7)

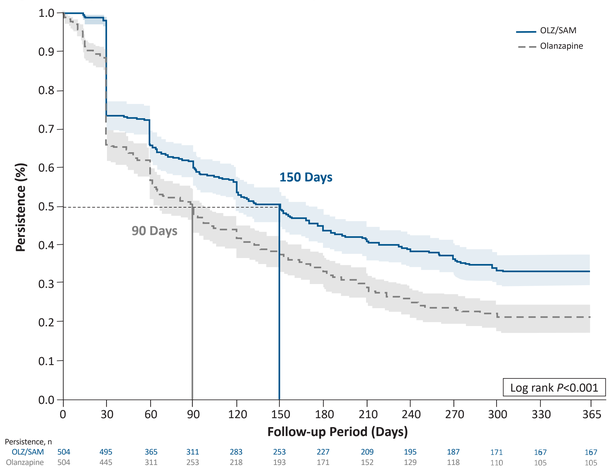
[a]Olanzapine was taken by 315 (62.5%) patients in the OLZ/SAM group during the baseline period.
LAI, long-acting injectable; OLZ/SAM, combination olanzapine and samidorphan.

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

Treatment Patterns

- At 12 months, 33.1% of patients were persistent on OLZ/SAM vs 20.8% on olanzapine
- Median days persistent: 150 days vs 90 days for OLZ/SAM vs olanzapine

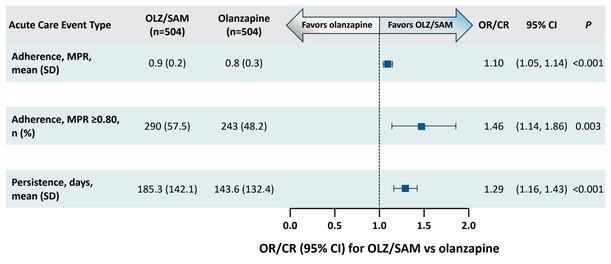
Figure 2. Kaplan-Meier Curves of Probability of Persistence



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 almost 50% lower with OLZ/SAM vs olanzapine (66.9% vs 79.2%, OR [95% CI]: 0.53 [0.40, 0.71], *P*<0.001)

Figure 3. Treatment Patterns[a]

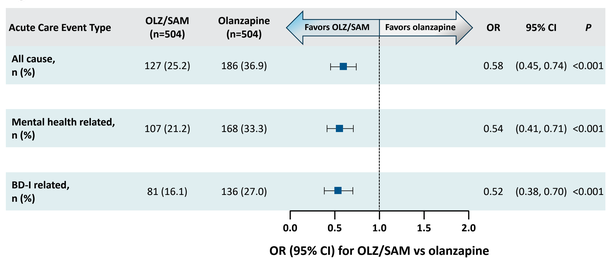


[a]Adherence and persistence are presented as CRs, MPR ≥0.80 as an OR.
CR, count ratio; MPR, medication possession ratio; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: IP Admissions

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

Figure 4. Percent of Patients With ≥1 IP Admission

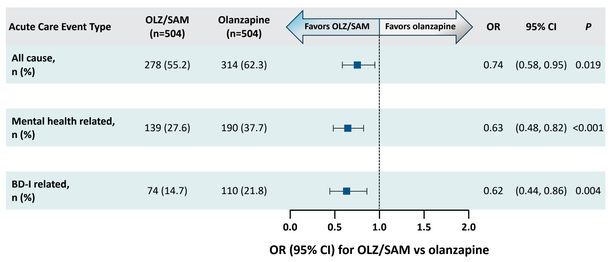


BD-I, bipolar I disorder; IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: ED Visits

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

Figure 5. Percent of Patients With ≥1 ED Visit

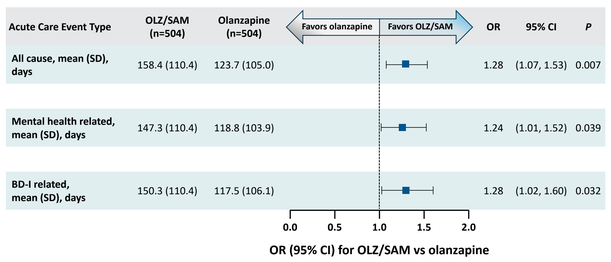


BD-I, bipolar I disorder; ED, emergency department; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: Number of Days to First IP Admission

- Across all-cause, mental health–related, and BD-I–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

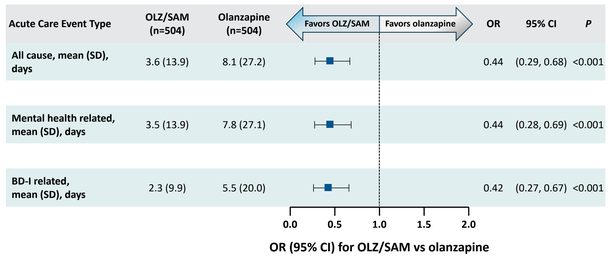


BD-I, bipolar I disorder; IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio.

Acute Care Events: Number of Days Hospitalized

- Across all-cause, mental health–related, and BD-I–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



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

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

46% higher odds of **being adherent** (MPR ≥0.80)
OR (95% CI): 1.46 (1.14, 1.86); *P*=0.003

47% lower odds of **discontinuation**
OR (95% CI): 0.53 (0.40, 0.71); *P*<0.001

92% higher odds of **being relapse-free**[a]
OR (95% CI): 0.52 (0.38, 0.70); *P*<0.001

[a]Calculated based on OR of BD-I–related IP admissions (used as a proxy for relapse); BD-I–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 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 performed 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 BD-I–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

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.

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, 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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