Acute Care Events Following Initiation of Olanzapine/Samidorphan Among Patients With Schizophrenia or Bipolar I Disorder and Comorbid Alcohol Use Disorder

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BACKGROUND

- The combination of olanzapine and samidorphan (OLZ/SAM) is approved in the United States for the treatment of adults with schizophrenia or bipolar I disorder (BD-I)[1]
- Alcohol use disorder (AUD) is a common comorbidity in these patients and is associated with increased risk of hospitalization[2,3]
- Samidorphan is an opioid receptor antagonist that was tested in a phase 2 study in patients with AUD
  - Although the study did not meet its primary endpoint, samidorphan treatment was associated with significant reductions in cumulative heavy drinking days and reductions in drinking-risk severity and alcohol craving[4]
- In prior real-world studies of patients with schizophrenia or BD-I, significant reductions in acute care events and significantly better treatment patterns versus olanzapine were observed following OLZ/SAM initiation[5-7]; here we describe outcomes in patients with comorbid AUD, a difficult-to-treat high-risk population

OBJECTIVE

- To assess and compare acute care events among patients with schizophrenia or BD-I and comorbid AUD in the 12 months before and after initiating OLZ/SAM

METHODS

Data Source

- Administrative claims data from October 18, 2020, to December 31, 2024, obtained from the Komodo Healthcare Map were analyzed retrospectively (**Figure 1**)
- The Komodo Healthcare Map is a fully deidentified US-based database with membership information for ~150 million patients covered by a commercial (66%), Medicaid (27%), or Medicare Advantage (7%) health plan

Patients and Study Design

Inclusion Criteria

- ≥1 pharmacy or medical claim for OLZ/SAM between October 18, 2021, and December 31, 2023
- Age ≥18 years with ≥1 medical claim for schizophrenia or BD-I during the baseline or follow-up period and ≥1 medical claim for AUD during the baseline period
  - Patients with medical claims for both schizophrenia and BD-I in the observation period were assigned to the schizophrenia cohort
- ≥12 months of continuous enrollment with medical and pharmacy benefits in the baseline period, before the index date (date of first medical or pharmacy claim for OLZ/SAM), and in the fixed follow-up period, beginning on and including the index date

Exclusion Criterion

- Any pharmacy or medical claim for OLZ/SAM during the baseline period

Outcomes

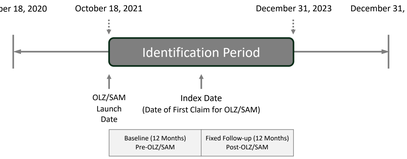
- Acute care events included inpatient (IP) admissions and emergency department (ED) visits in the all-cause, mental health–related, schizophrenia/BD-I–related, and AUD-related categories
  - IP admissions and ED visits were compared during the baseline and follow-up periods
- Treatment patterns
  - 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
- Patient demographics and baseline clinical characteristics and medication use

Statistics

- Baseline patient demographic and clinical characteristics and medication use are reported as numbers and percentages for categorical variables and mean (SD) for age
- Changes in the proportions of patients with ≥1 IP admission or ED visit between the baseline and follow-up periods were evaluated using an unadjusted pairwise comparison with McNemar's test

METHODS

Figure 1. Study Design



OLZ/SAM, combination olanzapine and samidorphan.

RESULTS

Table 1. Baseline Patient Demographics, Clinical Characteristics, and Medication Use

Characteristics	Schizophrenia and Comorbid AUD (N=326)	BD-I and Comorbid AUD (N=238)
Age, mean (SD), years	39.1 (11.5)	39.0 (11.7)
Female, n (%)	122 (37.4)	151 (63.5)
Insurance type, n (%)[a]		
Commercial	33 (10.1)	69 (29.0)
Medicaid	230 (70.6)	138 (58.0)
Medicare Advantage	60 (18.4)	31 (13.0)
Select health characteristics reported by ≥15% of patients in either cohort during baseline, n (%)		
Anxiety disorders	219 (67.2)	196 (82.4)
Major depressive disorder	160 (49.1)	139 (58.4)
Hypertension	145 (44.5)	81 (34.0)
Obesity	136 (41.7)	78 (32.8)
Posttraumatic stress disorder	97 (29.8)	103 (43.3)
Hyperlipidemia	92 (28.2)	66 (27.7)
Intentional self-inflicted injury	81 (24.8)	50 (21.0)
Type 2 diabetes mellitus	63 (19.3)	36 (15.1)
Antipsychotic use during baseline, n (%)[b]		
Any second-generation oral	310 (95.1)	218 (91.6)
Olanzapine	224 (68.7)	148 (62.2)
Any first-generation oral	92 (28.2)	29 (12.2)
Any second-generation LAI	70 (21.5)	15 (6.3)
Any first-generation LAI	20 (6.1)	1 (0.4)
None	6 (1.8)	15 (6.3)

[a]Values do not sum to 100% because none/unknown insurance type was identified in 0.92% of patients with schizophrenia and comorbid AUD. [b]Overall, the most common antipsychotics used in the baseline period (reported by >20% of patients in either cohort) were olanzapine, quetiapine, aripiprazole, and cariprazine.
AUD, alcohol use disorder; BD-I, bipolar I disorder; LAI, long-acting injectable.

Table 2. Adherence, Persistence, and Discontinuation

Follow-up[a] treatment patterns	Schizophrenia and Comorbid AUD (N=326)	BD-I and Comorbid AUD (N=238)
MPR, mean (SD)	0.86 (0.20)	0.85 (0.22)
MPR ≥0.80, %	58.3	56.3
Days persistent, mean (SD)	175.0 (134.1)	157.8 (138.1)
Discontinuation, %	74.2	74.0

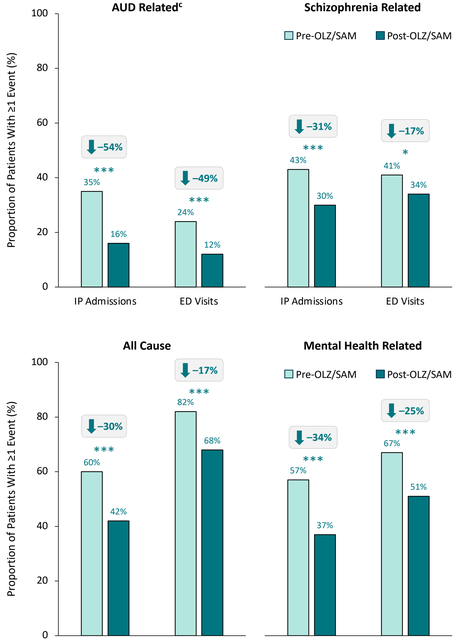
[a]The follow-up period began on the index date and ended 12 months after the index date.
AUD, alcohol use disorder; BD-I, bipolar I disorder; MPR, medication possession ratio.

RESULTS

Schizophrenia and Comorbid AUD

- For patients with schizophrenia and comorbid AUD, statistically significant reductions in the proportions of patients with ≥1 acute care event were observed across all categories in the 12 months after initiating OLZ/SAM treatment (**Figure 2**)

Figure 2. Acute Care Events[a,b]

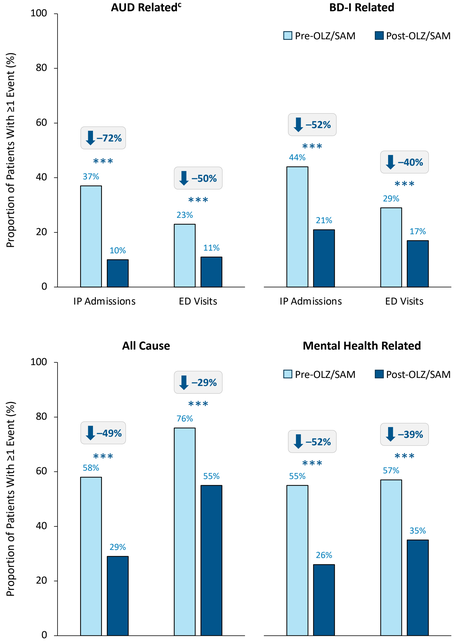


*P≤0.05 and ***P<0.001 for absolute difference.
[a]Absolute percentage point differences (95% CI): AUD-related IP admissions in patients with schizophrenia and comorbid AUD, −19% (−24%, −14%); AUD-related ED visits in patients with schizophrenia and comorbid AUD, −12% (−17%, −7%); schizophrenia-related IP admissions, −14% (−19%, −8%); schizophrenia-related ED visits, −7% (−13%, −1%); mental health–related IP admissions, −19% (−25%, −13%); mental health-related ED visits, −17% (−23%, −10%); all-cause IP admissions, −18% (−24%, −12%); all-cause ED visits, −14% (−20%, −8%). [b]Gray boxes show relative change from baseline to follow-up. [c]Events were defined as AUD related if the claim included an ICD-10-CM diagnosis code for AUD, including codes for alcohol abuse, dependence, intoxication, or withdrawal; alcohol-related medical conditions, including liver, neurologic, cardiovascular, gastrointestinal, pancreatic, and endocrine conditions; alcohol-related pregnancy conditions, including alcohol use during pregnancy and fetal effects; and alcohol-related counseling.
AUD, alcohol use disorder; ED, emergency department; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; IP, inpatient.

BD-I and Comorbid AUD

- For patients with BD-I and comorbid AUD, statistically significant reductions in the proportions of patients with ≥1 acute care event were observed across all categories in the 12 months after initiating OLZ/SAM treatment (**Figure 3**)

Figure 3. Acute Care Events[a,b]



***P<0.001 for absolute difference.
[a]Absolute percentage point differences (95% CI): AUD-related IP admissions in patients with BD-I and comorbid AUD, −26% (−33%, −20%); AUD-related ED visits in patients with BD-I and comorbid AUD, −11% (−17%, −6%); BD-I–related IP admissions, −23% (−31%, −16%); BD-I–related ED visits, −11% (−18%, −5%); mental health–related IP admissions, −29% (−37%, −21%); mental health–related ED visits, −22% (−30%, −15%); all-cause IP admissions, −28% (−36%, −21%); all-cause ED visits, −22% (−30%, −14%). [b]Gray boxes show relative change from baseline to follow-up. [c]Events were defined as AUD related if the claim included an ICD-10-CM diagnosis code for AUD, including codes for alcohol abuse, dependence, intoxication, or withdrawal; alcohol-related medical conditions, including liver, neurologic, cardiovascular, gastrointestinal, pancreatic, and endocrine conditions; alcohol-related pregnancy conditions, including alcohol use during pregnancy and fetal effects; and alcohol-related counseling.
AUD, alcohol use disorder; BD-I, bipolar I disorder; ED, emergency department; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; IP, inpatient.

Clinical context:

Initiating OLZ/SAM was associated with significant reductions in patients experiencing acute care events

Schizophrenia[a] and Comorbid AUD	IP Admissions	ED Visits
AUD related:	54%	49%
Schizophrenia related:	31%	17%

BD-I[b] and Comorbid AUD	IP Admissions	ED Visits
AUD related:	72%	50%
BD-I related:	52%	40%

[a]Absolute percentage point differences (95% CI): AUD-related IP admissions in patients with schizophrenia and comorbid AUD, −19% (−24%, −14%); AUD-related ED visits in patients with schizophrenia and comorbid AUD, −12% (−17%, −7%); schizophrenia-related IP admissions, −14% (−19%, −8%); schizophrenia-related ED visits, −7% (−13%, −1%). [b]Absolute percentage point differences (95% CI): AUD-related IP admissions in patients with BD-I and comorbid AUD, −26% (−33%, −20%); AUD-related ED visits in patients with BD-I and comorbid AUD, −11% (−17%, −6%); BD-I–related IP admissions, −23% (−31%, −16%); BD-I–related ED visits, −11% (−18%, −5%).
AUD, alcohol use disorder; BD-I, bipolar I disorder; ED, emergency department; IP, inpatient; OLZ/SAM, combination olanzapine and samidorphan.

LIMITATIONS

- The insured groups studied may not be representative of uninsured patients
- 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 treatment
- No adjustment for multiplicity was performed for the statistical tests used in these analyses
- AUD was identified from claims during the baseline period only; AUD status during the follow-up period may have varied across patients

CONCLUSIONS

- Initiating OLZ/SAM treatment was associated with statistically significant reductions in the proportions of patients with schizophrenia or BD-I and comorbid AUD with ≥1 AUD-related IP admission or ED visit
  - The numerically largest reductions were observed for AUD-related acute care events
- The significant reductions in all-cause, mental health–related, and schizophrenia/BD-I–related acute care events were consistent with those observed in prior real-world studies of OLZ/SAM[5-7]
- Findings were consistent across the schizophrenia and BD-I cohorts
- Significant reductions in AUD-related acute care events are of particular interest considering this difficult-to-treat high-risk patient population

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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.

AP has received consultant honoraria from Alkermes PLC, BMS, the Board of Psychedelic Medicine and Therapies, the California Institute of Integral Studies, Compass Pathways, Definium, the Fireside Project, the 1440 Foundation, Luciem, NACCME, and Otsuka; has served on advisory boards for AbbVie, Alkermes PLC, Definium Therapeutics, NACCME, Osmind, Otsuka, and Tactogen; and has received grant/research support from Filament, MAPS, and Usona.

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KB, MJD, and HRP are or were employees of Alkermes, Inc., and may own stock/options in the company.

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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