Hospitalizations in Adult Patients with Schizophrenia Treated with Oral Atypical Antipsychotics: A Real-World Study Using US Claims Data

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Introduction

- Oral atypical antipsychotics (OAAs) are recommended as first-line treatment for patients with schizophrenia (SCZ) by the American Psychiatric Association[1]; however, there is no guidance provided on which OAA to use.
- The OAA brexpiprazole was FDA-approved in 2015 for treatment in patients with SCZ, and an economic model estimated it was associated with lower cost and less healthcare utilization than some other OAAs[2].
- There are currently no real-world data available comparing hospitalizations between brexpiprazole and other OAAs in patients with SCZ.

Objective

To compare all-cause and psychiatric hospitalizations among adult patients with SCZ newly treated with brexpiprazole versus other US FDA-approved OAAs in a real-world setting.

Methods

- Retrospective cohort study using: (1) Truven Health MarketScan® Commercial (C), Medicare Supplemental (MS), and Multi-State Medicaid (M) Databases[a] and (2) de-identified Optum® Clinformatics® Datamart.
- Patient identification **(Figure 1)**
  - ≥1 inpatient or ≥2 outpatient claims for existing or newly diagnosed SCZ[b] in any diagnoses field during the study period (07/01/2014-09/30/2017 for MarketScan C/MS, and Optum; 07/01/2014-06/30/2017 for MarketScan M).
  - ≥1 pharmacy claim for brexpiprazole or another OAA (i.e. aripiprazole, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone) during the identification (ID) period (07/01/2015-09/30/2016 for MarketScan C/MS, and Optum; 07/01/2015-06/30/2016 for MarketScan M) with no claims for the same index therapy in the previous 12 months.
  - Index date: date of first OAA claim.
  - ≥1 diagnosis for SCZ during baseline (1 year prior to index date) or on the index date.
  - ≥18 years of age on index date.
  - Have continuous enrollment during baseline and follow-up (12 months after index date).
- Outcome measures (measured during 12-month follow-up)
  - Primary outcome: number of all-cause and psychiatric (claims with primary diagnosis for any mental health disorder [ICD-9-CM: 290.xx-311.xx; ICD-10-CM: F01.xx-F99.xx]) hospitalizations per year.
  - Secondary outcome: medication adherence measured by proportion of days covered (PDC).
- Statistical analysis
  - Negative binomial regression models were conducted to compare adjusted number of all-cause and psychiatric hospitalizations per year among OAAs (brexpiprazole vs. another individual OAA) in the follow-up, controlling for baseline demographics, clinical characteristics, medication use, and healthcare utilization.
  - Only statistically significant covariates (p<0.05) were presented in the final model results.
  - Data transformations and analyses were performed using SAS© version 9.4.

[a] MarketScan is a registered trademark of Truven Health Analytics, part of the IBM Watson Health business.
[b] ICD-9-CM: 295.xx, excluding 295.4x and 295.7x; or ICD-10-CM: F20x, excluding F20.81x.

Results

Figure 1. Patient Identification

Have ≥1 inpatient claim or ≥2 outpatient claims for SCZ during study period[a]
N = 73,969 MarketScan
N = 42,397 Optum

↓

Received a FDA-approved OAA in identification (ID) period[b]
N = 38,119 MarketScan
N = 23,424 Optum

↓

Newly started an FDA-approved OAA in ID period
N = 15,864 MarketScan
N = 12,969 Optum

↓

≥1 SCZ dx prior to or on the index date; continuously enrolled during baseline and follow-up period; ≥18 years old; and had no mono index therapy
N = 4,951 MarketScan
N = 1,769 Optum

↓

2 random duplicates removed from MarketScan and Optum database, and patients who initiated clozapine, asenapine, loxapine, iloperidone, or cariprazine due to small sample size
N = 4,616 MarketScan
N = 1,638 Optum

↓

N = 6,254
(4,616 MarketScan; 1,638 Optum)

SCZ: schizophrenia; dx: diagnosis
[a] Study period: 07/01/2014-09/30/2017 for MarketScan C/MS and Optum; 07/01/2014-06/30/2017 for MarketScan M
[b] ID period: 07/01/2015-09/30/2016 for MarketScan C/MS and Optum; 07/01/2015-06/30/2016 for MarketScan M

- The final study sample consisted of 6,254 patients with SCZ **(Table 1).**

Table 1. Patient Baseline Characteristics

	Brexpiprazole N=176 (2.8%)	Aripiprazole N=786 (12.6%)	Lurasidone N=523 (8.4%)	Olanzapine N=1,264 (20.2%)	Paliperidone N=453 (7.2%)	Quetiapine N=1,234 (19.7%)	Risperidone N=1,427 (22.8%)	Ziprasidone N=391 (6.3%)	P Value
Age, year, mean (SD) [median]	39.5 (14.3) [39]	43.2 (17.0) [43]	42.7 (15.5) [44]	44.5 (16.8) [45]	41.2 (15.1) [39]	46.9 (16.8) [48]	45.1 (17.2) [46]	42.2 (14.6) [44]	<0.001
Female	93 (52.8)	363 (46.2)	278 (53.2)	563 (44.5)	184 (40.6)	592 (48.0)	628 (44.0)	197 (50.4)	<0.001
Insurance type									<0.001
Commercial	62 (35.2)	233 (29.6)	148 (28.3)	279 (22.1)	86 (19.0)	201 (16.3)	299 (21.0)	84 (21.5)	
Medicaid	80 (45.5)	325 (41.3)	252 (48.2)	687 (54.4)	283 (62.5)	727 (58.9)	774 (54.2)	241 (61.6)	
Medicare	34 (19.3)	228 (29.0)	123 (23.5)	298 (23.6)	84 (18.5)	306 (24.8)	354 (24.8)	66 (16.9)	
Charlson Comorbidity Index, mean (SD) [median]	1.3 (2.0) [0]	1.5 (2.2) [0]	1.6 (2.3) [1]	1.5 (2.1) [1]	1.2 (1.9) [0]	1.9 (2.5) [1]	1.5 (2.3) [1]	1.7 (2.4) [1]	<0.001
Hypertension	71 (40.3)	349 (44.4)	248 (47.4)	613 (48.5)	202 (44.6)	675 (54.7)	702 (49.2)	209 (53.5)	<0.001
Any baseline ED visits	104 (59.1)	422 (53.7)	301 (57.6)	772 (61.1)	266 (58.7)	776 (62.9)	850 (59.6)	249 (63.7)	0.003
Any baseline hospitalization	80 (45.5)	440 (56.0)	274 (52.4)	808 (63.9)	236 (52.1)	680 (55.1)	889 (62.3)	221 (56.5)	<0.001
Non-index antipsychotic medications	168 (95.5)	585 (74.4)	427 (81.6)	851 (67.3)	404 (89.2)	816 (66.1)	803 (56.3)	297 (76.0)	<0.001
Psychiatric medications[a]	164 (93.2)	581 (73.9)	453 (86.6)	915 (72.4)	364 (80.4)	925 (75.0)	891 (62.4)	300 (76.7)	<0.001

Data presented as n (%), unless otherwise indicated.
[a] Mood stabilizers, antidepressants, antianxiety medications, sedatives or hypnotics.

Results (cont'd)

- Unadjusted all-cause hospitalization did not differ across all OAA groups; but brexpiprazole users had the lowest mean (SD) number of unadjusted psychiatric hospitalizations in the follow-up period (0.52 [1.0]; p=0.013).
- Controlling for differences in baseline characteristics, the adjusted number of all-cause and psychiatric hospitalizations did not differ when comparisons were made across all OAA groups **(Table 2)**.
- When compared to brexpiprazole users, other OAAs had 1.26~1.50 times more psychiatric hospitalizations per year, although the difference was only statistically significant between paliperidone and brexpiprazole users (p=0.032) **(Table 2)**.
- The overall unadjusted medication adherence was low in this population (%PDC≥0.8: 26.7%) but differed across treatment options (p<0.001), with paliperidone users having the lowest medication adherence (21.2%) and lurasidone having the highest (32.3%).

Table 2. Adjusted Incident Rate Ratio and Number of Hospitalizations per Year (95% CI)

Negative Binomial Models				
	Adjusted No. of All-Cause Hospitalizations per Year		Adjusted No. of Psychiatric[a] Hospitalizations per Year	
Index Treatment (Ref: Brexpiprazole)	**IRR (95% CI)**	**P Value**	**IRR (95% CI)**	**P Value**
Aripiprazole	1.17 (0.88 – 1.57)	0.281	1.32 (0.92 – 1.89)	0.129
Lurasidone	1.22 (0.90 – 1.65)	0.190	1.30 (0.90 – 1.88)	0.165
Olanzapine	1.20 (0.90 – 1.59)	0.212	1.37 (0.97 – 1.94)	0.075
Paliperidone	1.31 (0.96 – 1.77)	0.087	1.50 (1.04 – 2.19)	**0.032**
Quetiapine	1.23 (0.92 – 1.63)	0.157	1.33 (0.94 – 1.88)	0.110
Risperidone	1.15 (0.86 – 1.52)	0.345	1.26 (0.89 – 1.79)	0.186
Ziprasidone	1.31 (0.96 – 1.79)	0.089	1.46 (1.00 – 2.14)	0.050
	Adjusted No. of All-Cause Hospitalizations per Year (95% CI)		**Adjusted No. of Psychiatric[a] Hospitalizations per Year (95% CI)**	
Index treatment	P=0.595; df=7		P=0.451; df=7	
Aripiprazole	0.779 (0.689 – 0.880)		0.514 (0.442 – 0.598)	
Lurasidone	0.812 (0.701 – 0.940)		0.506 (0.423 – 0.606)	
Olanzapine	0.794 (0.723 – 0.872)		0.533 (0.476 – 0.598)	
Paliperidone	0.866 (0.743 – 1.010)		0.586 (0.487 – 0.704)	
Quetiapine	0.814 (0.740 – 0.895)		0.517 (0.460 – 0.583)	
Risperidone	0.760 (0.694 – 0.833)		0.492 (0.440 – 0.551)	
Ziprasidone	0.868 (0.739 – 1.021)		0.570 (0.468 – 0.694)	
Brexpiprazole	0.663 (0.508 – 0.866)		0.389 (0.280 – 0.541)	

IRR: incidence rate ratio
Final model covariates (p<0.05): age, gender, insurance type, Charlson Comorbidity Index (all-cause only), hypertension (all-cause only), any baseline ED visits, any baseline hospitalization, baseline non-index antipsychotic medications, baseline psychiatric medications use, and index treatment.
[a] Claims with a primary diagnosis of any mental disorder (ICD-9-CM: 290.xx-311.xx; ICD-10-CM code: F01.xx-F99.xx).

Conclusions

- Despite treatment, patients with SCZ had high adjusted number of hospitalizations per year (range: 0.67-0.87); this may indicate an unmet need in this population.
- Brexpiprazole users had fewer psychiatric hospitalizations than paliperidone users in the follow-up period. Possibly due to the small sample size of brexpiprazole users, the differences between other OAAs and brexpiprazole were not statistically significant.
- While treatment decisions are driven by a number of factors (e.g., clinical circumstances and drug costs), choice of OAAs may affect healthcare utilization in patients with schizophrenia.
- Payers may want to assess differences within their own data when making formulary decisions, as medication costs can differ across plans.
- Limitations
  - We controlled for observable demographic and clinical differences, but due to data limitations were unable to control for the observable clinical factors (e.g. disease severity) that may account for group differences.
  - Future studies with a larger sample size of brexpiprazole users are warranted.

References

1. Lehman AF, et al. *Am J Psychiatry.* 2004; 161(2 Suppl):1-56.
2. Aigbogun MS, et al. *Clin Outcomes Res.* 2018; 10:443-456.

Disclosures: Greene and Waters are employees of Otsuka Pharmaceutical Development and Commercialization, Inc., Princeton, NJ. Yan, Chang, Tarbox, and Broder are employees of Partnership for Health Analytic Research, LLC, Beverly Hills, CA. Houle is an employee of Lundbeck, LLC, Deerfield, IL. Funding for the study and this poster was received from Otsuka Pharmaceutical Development and Commercialization, Inc. and Lundbeck, LLC. Research was conducted by PHAR, LLC.

International Society for Pharmacoeconomics and Outcomes Research, May 18-22, 2019, New Orleans, LA, USA