Clinical Characteristics, Treatment Patterns, and Healthcare Resource Utilization of Patients Prescribed Aripiprazole Lauroxil Versus Oral Aripiprazole: A Retrospective Claims-Based Study

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BACKGROUND

- Nonadherence to oral medication is a known challenge among some patients with schizophrenia[1]
- Gaps in oral antipsychotic use are associated with an increased risk of hospitalization[2]
- Long-acting injectable (LAI) antipsychotic medications provide consistent medication exposure and are associated with greater adherence, lower discontinuation rates, and reduced acute healthcare resource utilization (HCRU) compared with oral antipsychotics[3-6]
- Aripiprazole lauroxil (AL) is an atypical LAI antipsychotic indicated for the treatment of adults with schizophrenia and is available with monthly, every-6-weeks, and every-2-months dosing options that can be paired with a separate 1-day initiation regimen[7,8]
- In previous real-world studies of patients with schizophrenia, treatment initiation with AL was associated with significant reductions in the numbers of mental health–related inpatient (IP) admissions and emergency department (ED) visits[9,10]

OBJECTIVE

- To compare demographic and clinical characteristics, treatment patterns, and HCRU among adults with schizophrenia initiating AL versus oral aripiprazole (OA)

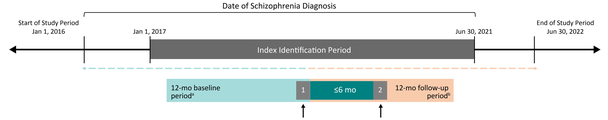
METHODS

Data Source

- Administrative claims data from January 1, 2016, to June 30, 2022, for privately or publicly insured persons across the United States obtained from the Merative™ MarketScan® Commercial Claims and Encounters (CCAE), Medicare Supplemental (MDCR), and Medicaid Multi-State (MDCD) research databases were analyzed retrospectively
  - The CCAE database includes approximately 62.9 million covered lives per year; the MDCR and MDCD databases represent 2.6 million and 16.8 million lives (over 3 years), respectively

Study Design and Patient Selection

Figure 1. Study Design



[a]Patients had to have ≥12 months of continuous enrollment before and ≥12 months of continuous enrollment after the index date; baseline medical history was based on the 12-month period before and inclusive of the index date. [b]The follow-up period from the index date (exclusive) to the date of disenrollment or end of study period allowed for a fixed 12 months of follow-up to assess treatment patterns and healthcare resource utilization. [c]Date of first aripiprazole lauroxil or oral aripiprazole claim on or after initial diagnosis date. [d]The second of 2 claims (pharmacy or medical) was required to be within 6 months of the first claim.

- Criteria for patient identification for this analysis are listed in **Figure 2**

Outcomes

- Demographics and baseline clinical characteristics by treatment group (AL or OA)
- Treatment patterns
  - *Discontinuation*: a continuous gap of ≥60 days without a claim for the index prescription following the therapeutic window for AL or after the previous claim's days' supply for OA
  - *Persistence*: the number of days from the index date to date of first discontinuation or end of the 1-year follow-up period, whichever occurred first
  - *Switching*: the presence of a claim for antipsychotic medication other than that initiated at index within the 60-day maximum allowable gap from the date of discontinuation
  - *Proportion of days covered (PDC)*: calculated as number of available days of index therapy divided by 365
  - *Adherent*: PDC ≥ 0.80
- HCRU outcomes
  - Proportions of patients with all-cause and mental health–related IP admissions and outpatient (OP) and ED visits
  - Utilization per patient per month (PPPM) for the outcomes listed above as well as all-cause OP pharmacy claims

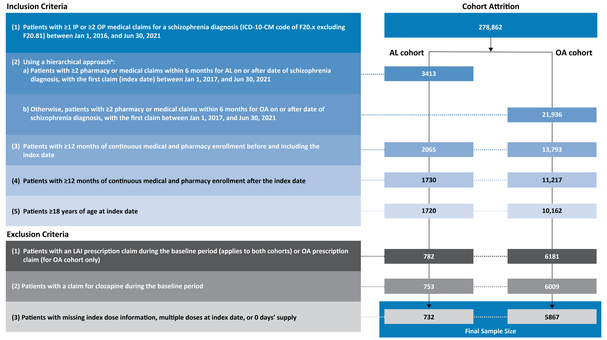
Statistical Analysis

- Propensity score matching (using a 1:1 matching ratio) was used to balance the treatment groups on 23 measured covariates (eg, age, sex, index year, and baseline HCRU)
- Treatment patterns
  - Persistence was compared between the matched AL and OA cohorts using a Cox proportional hazards model
  - Proportions adherent (PDC ≥ 0.80) were compared between the 2 matched cohorts using a logistic regression model
  - The other treatment pattern outcomes were analyzed descriptively
- HCRU
  - A logistic regression model was fitted to compare binary HCRU outcomes (occurrence of event, yes or no) between the 2 matched cohorts
  - A 2-part modeling strategy combining logistic and Poisson regression models was used to compare visit counts PPPM for each cohort and all-cause drug claims PPPM, yielding the estimated rate ratio (RR); bootstrapping was used for generating 95% CIs

RESULTS

- The total sample size was 6599 patients (AL cohort, n=732 patients; unmatched OA cohort, n=5867) (**Figure 2**, **Table 1**)

Figure 2. Patient Identification[a]



[a]Patients were categorized into the AL and OA cohorts using a hierarchical approach. If patients had ≥2 AL claims on or after the initial diagnosis date, they were included in the AL cohort; otherwise, patients were included in the OA cohort if they had ≥2 OA claims on or after the initial diagnosis date. [b]Maintaining patients with schizophrenia on treatment can be a clinical challenge. At least 2 claims were required to examine outcomes in the subset of patients across both treatment cohorts who may be more likely to benefit from treatment.
AL, aripiprazole lauroxil; ICD-10-CM, *International Classification of Diseases, Tenth Revision, Clinical Modification*; IP, inpatient; LAI, long-acting injectable; OA, oral aripiprazole; OP, outpatient.

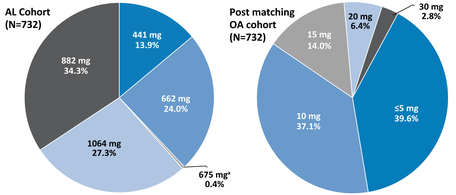
- Successful balancing of groups was achieved (standardized mean differences for all covariates <0.10) through propensity score matching with a 1:1 ratio (matched OA cohort, n=732)

Table 1. Patient Demographics and Baseline Clinical Characteristics Before Propensity Score Matching

Characteristics	AL Cohort (n=732)	OA Cohort (n=5867)
Age at index, mean (SD), years	37.3 (13.4)	39.7 (13.9)
Female, n (%)	323 (44.1)	2941 (50.1)
Year of index, n (%)		
2017	91 (12.4)	992 (16.9)
2018	105 (14.3)	1098 (18.7)
2019	196 (26.8)	1452 (24.7)
2020	234 (32.0)	1503 (25.6)
2021	106 (14.5)	822 (14.0)
Payer type, n (%)		
Commercial	45 (6.1)	882 (15.0)
Medicaid	683 (93.3)	4959 (84.5)
Medicare Supplemental	4 (0.5)	26 (0.4)
CCI, mean (SD)	0.88 (1.4)	1.08 (1.8)
Treatment history (past 12 months),[a] n (%)		
Typical oral antipsychotic	155 (21.2)	902 (15.4)
Atypical oral antipsychotic	627 (85.7)	3794 (64.7)
Oral aripiprazole	416 (56.8)	0
Mood stabilizer	386 (52.7)	3023 (51.5)
Antidepressant	494 (67.5)	4271 (72.8)
Anticholinergic	234 (32.0)	1703 (29.0)
Sedative/hypnotic	109 (14.9)	714 (12.2)
Antianxiety medication	325 (44.4)	2762 (47.1)
Stimulant/ADHD medication	197 (26.9)	1734 (29.6)

[a]Patients with ≥1 pharmacy claim during the 12-month baseline period.
ADHD, attention-deficit/hyperactivity disorder; AL, aripiprazole lauroxil; CCI, Charlson Comorbidity Index; OA, oral aripiprazole.

Figure 3. Index Prescription Dose



*Three patients had an index dose of 675 mg AL_{NCD} (initio), and their next AL claim had an unknown dose or was 675 mg.
AL, aripiprazole lauroxil; AL_{NCD}, NanoCrystal Dispersion formulation of AL; OA, oral aripiprazole.

- In the AL cohort, more patients were adherent to their medication compared with those in the matched OA cohort, and medication persistence was longer (**Table 2**)

Table 2. Treatment Patterns Among Matched Patient Cohorts

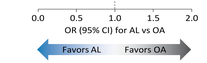
12-Month follow-up treatment patterns	AL Cohort (n=732)	Propensity Score–Matched OA Cohort (n=732)
Persistence, days, median (Q1, Q3)[a]	365.0 (154.0, 365.0)	153.0 (72.0, 365.0)
HR (95% CI) for nonpersistence, *P*[b]	0.5 (0.44, 0.56), <0.0001	
Switching, n (%)[c]	163 (22.3)	216 (29.4)
To oral antipsychotic	135 (18.4)	183 (24.9)
To LAI antipsychotic	28 (3.8)	33 (4.5)
PDC, mean (SD)[d]	0.72 (0.27)	0.51 (0.22)
Adherence (PDC ≥ 0.80), n (%)	369 (50.4)	176 (24.0)
OR (95% CI), *P*[b]	3.22 (2.57, 4.02), <0.0001	
Discontinuation, n (%)[e]	362 (49.5)	522 (71.4)

[a]Persistence was defined as number of days the from index date to date of first discontinuation or end of the 1-year follow-up period, whichever occurred first. [b]Reference = OA. [c]Switching was defined as the presence of a claim for antipsychotic medication other than that initiated at index within the 60-day maximum allowable gap period after the date of discontinuation. [d]PDC was calculated as number of available days of index therapy divided by 365. [e]Discontinuation was defined as a continuous gap of ≥60 days without a claim for the index prescription following the therapeutic window for AL or after the previous claim's days' supply for OA.
AL, aripiprazole lauroxil; HR, hazard ratio; LAI, long-acting injectable; OA, oral aripiprazole; OR, odds ratio; PDC, proportion of days covered; Q1, quartile number.

- Fewer patients in the AL cohort had all-cause IP and ED visits versus the OA cohort; odds of having ≥1 mental health–related IP visit were also significantly lower for patients who initiated AL (**Figure 4**)
- Numbers of all-cause and mental health–related IP and ED visits PPPM were significantly lower in the AL cohort versus the matched OA cohort (**Figure 5**)
- OP utilization did not differ between the matched cohorts

Figure 4. All-Cause and Mental Health–Related IP, OP, and ED Visits

HCRU Event	AL, n (%) (N=732)	Matched OA, n (%) (N=732)	OR[a]	95% CI	*P*
All Cause					
≥1 IP visit	253 (34.6)	302 (41.3)	0.75	(0.61, 0.93)	0.0079
≥1 ED visit	427 (58.3)	470 (64.2)	0.78	(0.63, 0.97)	0.0222
≥1 OP visit	727 (99.3)	731 (99.8)	0.27	(0.04, 1.80)	0.1741
Mental Health Related					
≥1 IP visit	232 (31.7)	280 (38.3)	0.75	(0.60, 0.93)	0.0082
≥1 ED visit	282 (38.5)	314 (42.9)	0.83	(0.68, 1.03)	0.0888
≥1 OP visit	695 (94.9)	705 (96.2)	0.73	(0.44, 1.21)	0.2280



[a]Reference = OA.
AL, aripiprazole lauroxil; ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; OA, oral aripiprazole; OP, outpatient; OR, odds ratio.

Figure 5. Numbers of All-Cause and Mental Health–Related IP, OP, and ED Visits, PPPM

HCRU Event	AL, mean (SD) (N=732)	Matched OA, mean (SD) (N=732)	RR[a]	95% CI[b]
All Cause				
Number of IP visits PPPM	0.08 (0.18)	0.09 (0.12)	0.83	(0.70, 0.97)
Number of ED visits PPPM	0.28 (0.57)	0.34 (0.49)	0.85	(0.72, 0.98)
Number of OP visits PPPM	7.03 (8.30)	7.50 (6.87)	0.94	(0.86, 1.03)
Mental Health Related				
Number of IP visits PPPM	0.07 (0.17)	0.08 (0.11)	0.84	(0.70, 0.98)
Number of ED visits PPPM	0.12 (0.29)	0.15 (0.26)	0.78	(0.65, 0.93)
Number of OP visits PPPM	3.34 (4.23)	3.62 (3.88)	0.93	(0.84, 1.03)

[a]Reference = OA. [b]The bootstrapping model conducted to compare counts PPPM between cohorts did not produce *P* values; CIs were reported for hypothesis testing.
AL, aripiprazole lauroxil; ED, emergency department; HCRU, healthcare resource utilization; IP, outpatient; OA, oral aripiprazole; OP, outpatient; PPPM, per patient per month; RR, rate ratio.

LIMITATIONS

- Requiring ≥12 months of continuous enrollment before and after the index date may have limited the sample size
- Requiring 2 claims of AL and OA may have increased estimates of adherence and persistence; however, the requirement was the same for both cohorts
- Claims related to schizophrenia and its treatment may not have been captured accurately or completely, which could have led to inaccurate reports of treatment patterns and an underestimation of HCRU

CONCLUSIONS

- In this real-world study of patients with schizophrenia, patients initiating AL were more likely to be adherent to treatment and had longer medication persistence compared with patients initiating OA
- AL was associated with significantly reduced odds of all-cause IP and ED visits and mental health–related IP visits versus OA
  - Numbers of visits to OP settings were similar between AL and OA
- All-cause and mental health–related IP admissions and ED visits PPPM were also significantly reduced among patients initiating AL versus OA
- Future investigations may explore whether the improved adherence and persistence and concurrent reductions in acute HCRU associated with use of LAI AL versus OA translate into lower rates of relapse and reduced physical, psychosocial, and economic burden experienced by patients with schizophrenia

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DISCLOSURES

JMK has been a consultant for or received honoraria from Alkermes, Boehringer Ingelheim, Click Therapeutics, Intra-Cellular Therapies, Janssen, Johnson & Johnson, Karuna, LB Pharmaceuticals, Lundbeck, Lyndra, Merck, Neurocrine Biosciences, Newron, Otsuka, Pierre Fabre, Reviva, Roche, Saladax, Sunovion, Takeda, and Teva; has received grant support from Janssen, Lundbeck, and Otsuka; and is a shareholder of LB Pharmaceuticals and Vanguard Research Group

ABB, CL, ZW, and **ESN** have nothing to disclose

LNS, MJD, and **RG** are or were employees of Alkermes, Inc., and may own stock/options in the company

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