# Treatment Patterns and Healthcare Resource Utilization of Patients Early in Schizophrenia Illness Initiating Aripiprazole Lauroxil Versus Oral Aripiprazole: A Retrospective Claims-Based Study

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## BACKGROUND

- Optimal treatment of patients with schizophrenia, including those who are early in the course of their illness, has the potential to provide long-term benefits[1]
- Early initiation of treatment with long-acting injectable (LAI) antipsychotic medications, which provide consistent medication exposure over various dosing intervals,[2] may improve clinical and real-world outcomes in patients with schizophrenia[3-5]
- In a real-world study, patients with schizophrenia initiating the atypical LAI antipsychotic aripiprazole lauroxil[6] (AL) were more likely to be adherent to treatment, had longer medication persistence, and had reduced odds of acute healthcare resource utilization (HCRU) compared with a propensity score–matched cohort initiating oral aripiprazole (OA)[7]
  - The secondary objective of the real-world study was to assess these same outcomes in a subgroup of patients with schizophrenia who were early in their illness

## OBJECTIVE

- This subgroup analysis compared real-world treatment patterns and HCRU among early-in-illness patients with schizophrenia initiating AL or OA

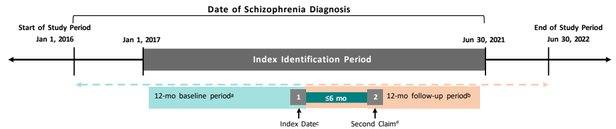
## METHODS

### 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, Medicare Supplemental, and Medicaid Multi-State research databases were analyzed retrospectively

### 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.

- "Early-in-illness" patients were defined as those aged 18–40 years who initiated the index treatment ≤1 year after their first observed schizophrenia diagnosis
- Criteria for identifying patients for the study and the early-in-illness subgroup are listed in **Figure 2**

### Outcomes

- 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
  - Proportions of patients with all-cause and mental health–related inpatient (IP) admissions and outpatient (OP) and emergency department (ED) visits
  - Average utilization per patient per month (PPPM) for the outcomes listed above as well as all-cause OP pharmacy claims

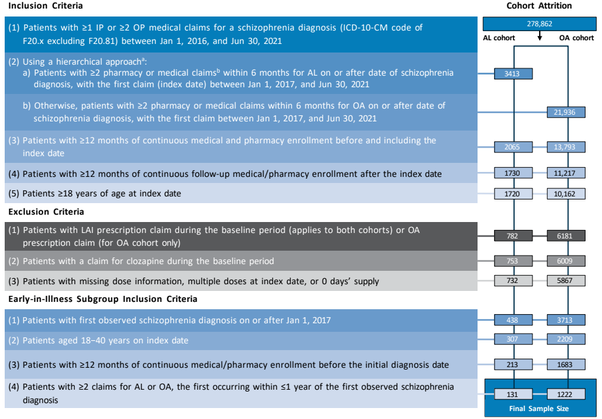
### Statistical Analysis

- Propensity score matching (using a 1:1 matching ratio) was used to balance the treatment groups on 22 measured covariates (eg, age, sex, index year, and baseline HCRU)
- Treatment patterns
  - Persistence was compared between the matched AL and OA early-in-illness cohorts using a Cox proportional hazards model
  - Proportions adherent (PDC ≥ 0.80) were compared between the 2 matched cohorts using a logistic regression model
  - Other treatment pattern outcomes were analyzed descriptively
- HCRU
  - A logistic regression model compared 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 between the 2 matched cohorts, yielding the estimated rate ratio (RR); bootstrapping was used for generating 95% CIs

## RESULTS

- Of the 6599 patients in the overall analysis, 1353 (20.5%) patients met the early-in-illness subgroup criteria (AL cohort, n=131; unmatched OA cohort, n=1222)

**Figure 2.** Patient Identification




[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.

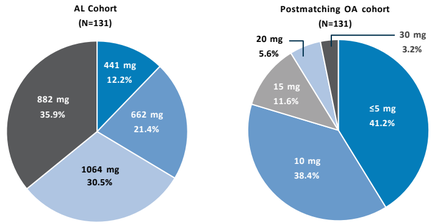
**Table 1.** Patient Demographics and Baseline Clinical Characteristics Before Propensity Score Matching

| Characteristics | AL Cohort (n=131) | OA Cohort (n=1222) | *P* Value |
|---|---|---|---|
| Age at index, mean (SD), years | 27.2 (6.4) | 27.2 (6.7) | 0.97 |
| Sex, female, n (%) | 51 (38.9) | 575 (47.1) | 0.08 |
| Year of index, n (%) | | | 0.010 |
| 2017 | 16 (12.2) | 198 (16.2) | |
| 2018 | 19 (14.5) | 258 (21.1) | |
| 2019 | 26 (19.9) | 302 (24.8) | |
| 2020 | 48 (36.6) | 289 (23.6) | |
| 2021 | 22 (16.8) | 175 (14.3) | |
| Payer type, n (%) | | | 0.001 |
| Commercial | 17 (13.0) | 313 (25.6) | |
| Medicaid | 114 (87.0) | 909 (74.4) | |
| CCI, mean (SD) | 0.51 (1.0) | 0.53 (1.1) | 0.82 |
| CCI category, 3+, n (%) | 8 (6.1) | 71 (5.8) | |
| Treatment history,[a] n (%) | | | |
| Typical oral antipsychotic | 21 (16.0) | 121 (9.9) | 0.03 |
| Atypical oral antipsychotic | 104 (79.4) | 720 (58.9) | <0.001 |
| Oral aripiprazole | 76 (58.0) | 0 | |
| Mood stabilizer | 53 (40.5) | 499 (40.8) | 0.93 |
| Antidepressant | 74 (56.5) | 832 (68.1) | 0.007 |
| Anticholinergic | 31 (23.7) | 250 (20.5) | 0.39 |
| Sedative/hypnotic | 10 (7.6) | 114 (9.3) | 0.52 |
| Antianxiety medication | 59 (45.0) | 548 (44.8) | 0.97 |
| Stimulant/ADHD medication | 31 (23.7) | 325 (26.6) | 0.47 |

[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.

- Successful balancing of groups was achieved (standardized mean differences for all covariates <0.10) through propensity score matching with a 1:1 ratio

**Figure 3.** Index Prescription Dose




AL, aripiprazole lauroxil; OA, oral aripiprazole.

- Among early-in-illness patients, the AL cohort had significantly higher adherence and significantly longer persistence with their medication compared with those in the matched OA cohort (**Table 2**)
- During 12 months of follow-up, fewer patients in the AL cohort discontinued treatment compared with patients in the matched OA cohort

**Table 2.** Treatment Patterns Among Matched Early-in-Illness Patient Cohorts

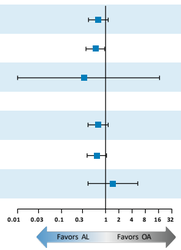
| 12-Month follow-up treatment patterns | AL Cohort (n=131) | OA Cohort (n=131) |
|---|---|---|
| **Persistence, median (Q1, Q3)[a]** | 256 (141, 365) | 123 (60, 298) |
| HR (95% CI) for nonpersistence, *P*[b] | 0.5 (0.38, 0.64), <0.0001 | |
| **Switching, n (%)[c]** | 29 (22.1) | 28 (21.1) |
| To oral antipsychotic | 27 (20.6) | 19 (14.6) |
| To LAI antipsychotic | 2 (1.5) | 9 (6.5) |
| **PDC, mean (SD)[d]** | 0.69 (0.27) | 0.47 (0.22) |
| **Adherence (PDC ≥ 0.80), n (%)** | 58 (44.3) | 27 (20.7) |
| OR (95% CI), *P*[b] | 3.0 (1.76, 5.24), <0.0001 | |
| **Discontinuation, n (%)[e]** | 73 (55.7) | 98 (75.1) |

[a]Persistence was defined as number of days 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.

- The odds of having ≥1 all-cause ED visit were 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 vs matched OA cohort (**Figure 5**)
- OP utilization did not differ between the matched cohorts

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

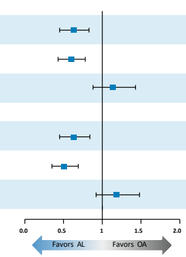
| HCRU Events | AL, n (%) (n=131) | Matched OA, n (%) (n=131) | OR[a] | 95% CI | *P* Value |
|---|---|---|---|---|---|
| **All Cause** | | | | | |
| ≥1 IP visit | 38 (29.0) | 49 (37.3) | 0.69 | (0.41, 1.15) | 0.16 |
| ≥1 ED visit | 63 (48.1) | 80 (61.2) | 0.59 | (0.36, 0.96) | 0.03 |
| ≥1 OP visit | 130 (99.2) | 131 (99.8) | 0.33 | (0.01, 16.84) | 0.58 |
| **Mental Health Related** | | | | | |
| ≥1 IP visit | 36 (27.5) | 47 (35.8) | 0.68 | (0.40, 1.15) | 0.15 |
| ≥1 ED visit | 42 (32.1) | 56 (42.8) | 0.63 | (0.38, 1.05) | 0.07 |
| ≥1 OP visit | 127 (97.0) | 125 (95.6) | 1.48 | (0.40, 5.41) | 0.55 |




[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, ED, and OP Visits, PPPM

| HCRU Events | AL, mean (SD) (n=131) | Matched OA, mean (SD) (n=131) | RR[a] | 95% CI[b] |
|---|---|---|---|---|
| **All Cause** | | | | |
| Number of IP visits PPPM | 0.04 (0.08) | 0.07 (0.10) | 0.63 | (0.45, 0.83) |
| Number of ED visits PPPM | 0.17 (0.31) | 0.28 (0.34) | 0.60 | (0.43, 0.78) |
| Number of OP visits PPPM | 5.37 (7.03) | 4.76 (4.62) | 1.14 | (0.88, 1.43) |
| **Mental Health Related** | | | | |
| Number of IP visits PPPM | 0.04 (0.08) | 0.07 (0.10) | 0.63 | (0.45, 0.84) |
| Number of ED visits PPPM | 0.07 (0.16) | 0.14 (0.20) | 0.50 | (0.35, 0.69) |
| Number of OP visits PPPM | 2.91 (3.74) | 2.49 (2.45) | 1.18 | (0.92, 1.48) |




[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, inpatient; OA, oral aripiprazole; OP, outpatient; PPPM, per patient per month; RR, rate ratio.

## LIMITATIONS

- The first diagnosis of schizophrenia captured in this database may not have been the patient's true initial diagnosis; age was restricted to increase the likelihood of patients included in the early-in-illness population being truly early in their illness
- Requiring ≥2 claims of AL and OA may have increased estimates of adherence and persistence; however, both cohorts had the same requirement
- 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, early-in-illness patients with schizophrenia initiating AL were more likely to be adherent to treatment and had longer medication persistence compared with matched patients initiating OA
- Initiating AL vs OA was associated with significantly reduced odds of all-cause ED visits
- All-cause and mental health–related IP admissions and ED visits PPPM were significantly reduced among early-in-illness patients initiating AL vs OA, whereas the numbers of visits in OP settings were similar between cohorts
- Future investigations exploring whether improvements in treatment patterns and reductions in acute HCRU early in schizophrenia are associated with better long-term outcomes and reduced economic burden are warranted

## REFERENCES

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

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***Key Contributors***

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the poster; gave final approval of the version to be presented; and agree to be accountable for all aspects of the work.

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