A comparison of oral aripiprazole with an ingestible sensor to oral atypical antipsychotic treatment in a real-world setting for the risk of hospitalization in adults with schizophrenia

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RWD84

INTRODUCTION

- Clinical trials are the cornerstone of rigorous identification of drug-related clinical outcomes.
- However, patients enrolled in these trials may not be fully representative of patients in the real world.
- Real-world data (RWD) can address this gap by supporting and supplementing the findings of clinical trials.
- This study compared patients with schizophrenia from an existing trial[1] to a real-world cohort prescribed oral atypical antipsychotics (OAAs), thereby demonstrating the clinical utility of RWD.

OBJECTIVE

- To compare the risk of psychiatric hospitalization for adults with schizophrenia treated with aripiprazole tablets with ingestible sensor (AS) vs those who received OAA treatment in a real-world setting.

METHODS

- An RWD platform, NeuroBlu,[2] was used to develop a retrospective cohort of adults with schizophrenia from the US MindLinc Electronic Health Record (EHR), with inclusion and exclusion criteria designed to mirror the completed single-arm, phase 3b, mirror-image trial (the AS trial).[1]
- This real-world cohort was compared to adults with schizophrenia who had participated in the AS trial. The index date for the real-world cohort was the date 6 months after OAA treatment initiation.
- The mirror-image–designed AS trial evaluated hospitalization rates in patients who used AS for up to 6 months compared to the same patients who used an OAA in the lookback period.
- The AS trial used modified intent-to-treat (mITT) reporting, with the main objective to identify whether AS reduced future psychiatric hospitalizations in adults with schizophrenia.

Study inclusion criteria for the RWD cohort:

- Patients aged 18–65 years
- Had ≥ 2 records of ICD-9/10 diagnosis of schizophrenia
- Had ≥ 1 psychiatric hospitalization within a 4-year period before the index date
- Prescribed an OAA for a total of ≥ 9 months (6 months pre- and ≥ 3 months post-index).

Study exclusion criteria for the RWD cohort:

- Prescription of a long-acting injectable (LAI) antipsychotic within 6 months pre- and 3 months post-index
- Individuals with any of the following diagnoses: bipolar I disorder; major depressive disorder; delirium; dementia; amnestic or other cognitive disorders; and those diagnosed with borderline, paranoid, histrionic, or antisocial personality disorder within 6 months pre- and 3 months post-index
- Record of an inpatient visit within 10 days before and after the index date.

- Propensity scoring using the nearest-neighbor algorithm was used to balance clinically important covariates across the AS and RWD cohorts and produce matched pairs on a 1:1 basis.
- These covariates were selected using stepwise regression techniques and clinical judgment from qualified psychiatrists.
- Standardized mean differences (SMDs) were used for covariate balance diagnostics, with SMD values < 0.1 considered representative of good covariate balance.
- Retrospective hospitalizations within 6 and 3-months pre-index were ascertained for both cohorts. The primary outcome was the number needed to treat (NNT) to prevent a psychiatric hospitalization within 3 months post-index.
- McNemar's tests were used to compare pre- and post-index hospitalizations for the AS trial and RWD cohort.

RESULTS

- Six variables were identified for cohort matching: baseline Clinical Global Impression – Severity of Illness scale (CGI-S), duration of psychiatric hospitalization, age, sex, race, and baseline OAA dose.
- These covariates were well balanced (SMD < 0.1) across cohorts (mean: 0.041; maximum SMD: 0.08).
- Cohort balancing using these 6 variables successfully identified 95 patients out of 113 total patients from the AS cohort to match 95 patients from the RWD cohort. **Figure 1** shows a plot of the SMDs across the selected clinically important covariates. **Table 1** shows the main baseline covariates for patients from AS and RWD cohorts who were 1:1 matched.
- McNemar's tests for the pre- and post-index differences in hospitalizations between groups were significant ($P = 0.004$ and $P = 0.001$ for the AS trial and RWD arm, respectively).
- NNT to prevent a psychiatric hospitalization for the AS cohort was 9 (95% confidence interval [CI] 6–20). **Table 2** shows the pre- and post-index hospitalization rates.

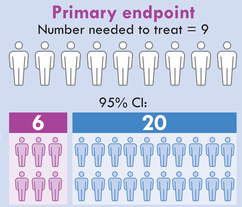
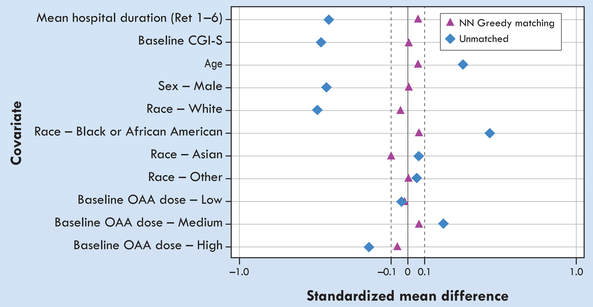


Figure 1. A Love plot with standardized mean differences across 6 clinically important variables before and after matching.



CGI-S, Clinical Global Impression – Severity of Illness scale; NN, nearest neighbor; OAA, oral atypical antipsychotic; Ret, retrospective.

Table 1. Descriptive and comparative statistics of matched pairs across matched variables.

	Matched patients treated with AS (n = 95)	Matched patients treated with OAA (n = 95)	Test statistic	*P* value
Age at index date (years)			0.182	0.67
Mean (SD)	44.9 (12.9)	44.1 (12.7)		
Median (IQR)	48 (34–56)	47 (33–54)		
Gender, n (%)			0	1
Female	53 (55.8)	53 (55.8)		
Male	42 (44.2)	42 (44.2)		
Race, n (%)			N/A	0.935
Asian	1 (1.1)	2 (2.1)		
Black or African American	56 (58.9)	53 (55.8)		
Other	2 (2.1)	2 (2.1)		
White	36 (37.9)	38 (40.0)		
Baseline CGI-S			0.817	0.366
Mean (SD)	3.82 (0.68)	3.82 (1.24)		
Median (IQR)	4 (3–4)	4 (3–5)		
Baseline OAA dose			0.272	0.873
Low	13 (13.7)	15 (15.8)		
Medium	42 (44.2)	43 (45.3)		
High	40 (42.1)	37 (38.9)		
Duration of psychiatric hospitalizations(months1–6 pre-index), days			5.62	0.018
Mean (SD)	1.3 (4.0)	1.1 (2.5)		
Median (IQR)	0 (0–0)	0 (0–1)		

AS, aripiprazole tablets with ingestible sensor; CGI-S, Clinical Global Impressions – Severity of Illness scale; IQR, interquartile range; N/A, not available; OAA, oral atypical antipsychotic; SD, standard deviation.

Table 2. Psychiatric hospitalization rates for AS and RWD cohorts before and after the index date.

Hospitalizations, n (%)	AS cohort (n = 95)	RWD cohort (n = 95)
Pre-index (–6 to –3 months)	10 (10.5)	29 (30.5)
Post-index (0 to 3 months)	0 (0)	11 (11.6)

AS, aripiprazole tablets with ingestible sensor; RWD, real-world data.

DISCUSSION

- These results demonstrated that cohort balancing techniques can be leveraged successfully to identify an appropriate real-world comparator to clinical trial patients.
- Based on the NNT results and baseline matched characteristics, we observed a similar trend in the impact on the psychiatric hospitalization rates among the AS and RWD cohorts.
- Hospitalization outcomes in this study were only assessed up to 3 months post-index; thus, longer follow-up times would be important in future research to properly differentiate AS from standard antipsychotic therapy.

CONCLUSIONS

- RWD provides a valuable resource in the exploration of clinical and health economic outcomes associated with the use of novel psychiatric treatment.
- The findings of this analysis provide preliminary support for the use of antipsychotics with ingestible sensors in the reduction of healthcare resource utilization.

References

1. Cohen EA, et al. *J Clin Psychiatry*. 2022;83(3):40541.
2. Patel R, et al. *BMJ Open*. 2022;12(4):e057227.

Disclosures

DHB, **SB**, and **JMC** are employees of Otsuka Pharmaceutical Development & Commercialization, Inc. **MMC**, **RA**, **CL**, **ST**, **MO**, and **JS** are employees of Holmusk Technologies, Inc., which received funding from Otsuka Pharmaceutical Development & Commercialization, Inc. to conduct this research.

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