Real-World Insights Into Long-Acting Injectable Antipsychotic Agent Initiation in the Inpatient Setting and Transition/Continuation of Care: Impact of LAI Characteristics on Outcomes Among Patients With Schizophrenia

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Introduction

- Schizophrenia is a chronic, debilitating psychiatric disorder primarily treated withantipsychotics[1]
- Most oral antipsychotics (OAs) are taken daily; long-acting injectable antipsychotics (LAIs) are given less often[2]
- LAIs are associated with better outcomes and adherence compared with OAs; however, little is known about how LAI-based treatment choices affect transition and continuation of care following hospitalization[3]
  - Transition of care encompasses how patients are treated across different clinical settings
  - Continuation of care encompasses how patients are treated after hospital discharge

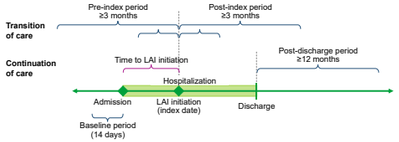
Objective

- To generate real-world insights into LAI prescribing patterns and their associations with transition and continuation of care in schizophrenia

Methods

- Adults with a schizophrenia diagnosis who initiated a LAI in an inpatient setting were identified using NeuroBlu, a database (DB) of electronic health record (EHR) data from United States (US) mental healthcare professionals operating MindLinc EHR
- Index date was defined as the date of first LAI treatment in the inpatient setting (ie, hospitalization) recorded in the NeuroBlu DB (**Figure 1**)
  - The cohort included patients discharged taking LAIs only and patients discharged taking LAIs together with OAs
  - For transition-of-care analyses, the pre-index period was defined as ≥3 to 12 months before LAI initiation/index date, and the post-discharge period was defined as ≥3 to 12 months after discharge from the hospital
  - For continuation-of-care analyses, the post-discharge period was defined as 12 months after hospital discharge

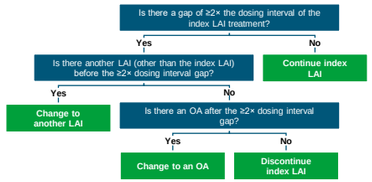
Figure 1. Study Design



Endpoints

- Transition-of-care endpoints included time to and rate of rehospitalization (hazard ratio; HR), and number of outpatient visits (incidence rate ratio; IRR) post-discharge
- Continuation-of-care endpoints included first treatment path after discharge, time to index LAI discontinuation, and number of patients who restart LAI/supplement with OA
  - **Figure 2** indicates the decision tree to determine the first treatment path after discharge; patients could continue index LAI, change to another LAI, change to an OA, or discontinue index LAI

Figure 2. Possible Treatment Paths After Discharge



Statistical Analysis

- For descriptive comparisons, chi-square or Fisher exact tests were used for categorical variables and Welch unpooled variance *t* test or Mann-Whitney *U* test for continuous variables
- To compare outcomes between patients who initiated different types of LAI treatments, a Cox regression model was used for time to rehospitalization and a generalized linear model for rehospitalization rate

Results

Patients

- Among patients included in NeuroBlu DB (n=538,565), 1197 met inclusion criteria and were included in these analyses (**Table 1**)
- Transition of care was assessed for patients (n=339) with ≥3 months of pre-index and post-index data. Continuation of care was evaluated for patients (n=449) with ≥12 months of post-index data (**Table 1**)
- Most of the population were aged 18–34 years, Black, male, and from the Northeast US (**Table 2**)

Table 1. Selection of Study Population

	Total	
Patients in the NeuroBlu DB	538,565	
Patients from clinical sites with inpatient and outpatient facilities	467,207	
Patients with a record of ICD-9/10 diagnosis of schizophrenia	13,018	
Patients prescribed LAI after schizophrenia diagnosis	2450	
Patients aged ≥18 years at index	2437	
Main cohort: patients who initiated LAI in an inpatient setting	1197	
Cohorts	Transition of care	Continuation of care
Patients with ≥3 months of pre- and post-index data[a]	339	–
Patients with ≥12 months post-discharge data	–	449

[a]260 patients from the transition of care group was included in the continuation of care group as well

Table 2. Patient Demographics at Index

Variable		Total n=1197
Sex, n (%)	Male	794 (66.3)
	Female	401 (33.5)
	Unknown	2 (0.2)
Age (years), mean (SD) [median]		40.2 (14.2) [39.0]
Race, n (%)	Black	558 (46.6)
	White	315 (26.3)
	Other[a]	108 (9.0)
	Unknown	216 (18.1)
US region,[a] n (%)	Northeast	744 (63.5)
	South	301 (25.7)
	Midwest	117 (10.0)
	West	9 (0.8)
Psychiatric comorbidity, n (%)	Substance use disorder	374 (31.2)
	Schizoaffective disorder	334 (27.9)
	Bipolar disorder	150 (12.5)
	Major depressive disorder	71 (5.9)
	Personality disorders	71 (5.9)
	Post-traumatic disorder	23 (1.9)
	Obsessive-compulsive disorder	9 (0.8)
	Dementia	9 (0.8)
	Delirium	7 (0.6)
	Attention deficit/hyperactivity disorder	5 (0.4)
	Generalized anxiety disorder	4 (0.3)
	Amnesia	1 (0.1)

[a]Region data missing for 26 patients.

Key Results

Treatment Patterns During Hospitalization

- At admission, 157 patients were taking atypical OAs (36% risperidone), 31% had substance use disorder, and 70% had a prior psychiatric hospitalization record; of 887 patients with Clinical Global Impression-Severity (CGI-S) data, 33.7% were severely ill (CGI-S score 6–7) (**Table 3**)
- Between admission and LAI initiation, 538 patients were given atypical OAs (50% risperidone)
- On average, LAIs were administered 7 days post-admission; the most prescribed index LAIs were haloperidol, dosed once monthly (49.2%), and risperidone, dosed once every 2 weeks (18.2%) (**Table 3**)
- Even though there was a shift toward use of second-generation antipsychotics across time periods, haloperidol usage remained high (63% in 1999–2004 and 45% in 2015–2020), compared with fluphenazine (28% in 1999–2004 and 8% 2015–2020), for example
- In hospital, 73.4% of patients were co-prescribed an OA with LAI; at discharge, 44.6% of patients were co-prescribed an OA

Transition of Care

- Among patients with ≥3 months of pre- and post-discharge data (n=339), 74% of patients co-prescribed an OA at discharge were rehospitalized within 12 months vs 69% prescribed LAI only (**Figure 3**)
- At post-discharge, patients taking LAIs had less risk of rehospitalization (HR, 0.49 [95% CI, 0.35–0.69]), and fewer outpatient visits (IRR, 50% [95% CI, 0.36–0.70]) than those co-prescribed an OA. There was no significant difference in number of outpatient visits between patients on LAIs dosed once monthly or less compared with LAIs dosed more often than once monthly

Continuation of Care

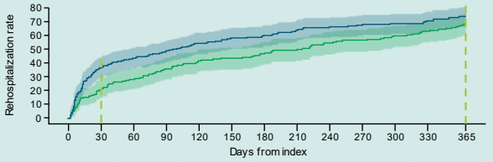
- By 12 months post-discharge, fewer patients (75.3%) discontinued an index LAI dosed once monthly or less often than an LAI dosed more often (86.5%) (**Table 4**)
- The median time to discontinuation of index LAI was 67 days (IQR, 60–91) when dosed once monthly or less often and 32 days (28–49) when dosed once every 2 weeks
- At discharge, a larger proportion of patients co-prescribed OA (46%) versus LAI alone (27%) showed improvements in CGI-S; however, most of these patients were severely ill at admission, compared with LAI alone

Table 3. Clinical Characteristics and Treatment Patterns During Hospitalization

			Total n=1197
Number of unique OAs prescribed before the index LAI, mean (SD) [median]			1.4 (1.4) [1]
CGI-S at admission[a]	Mean (SD) [median]		5 (1.0) [5]
	Category, n (%)	1–3 (normal to mildly ill)	47 (5.3)
		6–7 (severely to most ill)	299 (33.7)
		4–5 (moderately to markedly ill)	541 (61.0)
Index hospitalization length of stay (days), mean (SD) [median]			15.7 (22.8) [10]
Time from LAI initiation (index) to discharge (days), mean (SD) [median]			8.4 (18.4) [3]
Index LAI, n (%)		Haloperidol q1m	589 (49.2)
		Risperidone q2w	218 (18.2)
		Fluphenazine q4w–q6w	207 (17.3)
		Paliperidone palmitate q1m	125 (10.4)
		Aripiprazole q1m	52 (4.3)
		Olanzapine q2w–q4w	5 (0.4)
		Aripiprazole lauroxil q2m	1 (0.1)
Index year/year of LAI initiation, n (%)		2010–2014	517 (43.2)
		2015–2020	328 (27.4)
		2005–2009	254 (21.2)
		1999–2004	98 (8.2)
OA co-prescribed with index LAI, n (%)			878 (73.4)
First-generation/typical OA, n (%)			524 (43.8)
Second-generation/atypical OA, n (%)			570 (47.6)
Most common second-generation/atypical OA		Risperidone	248 (20.7)
		Quetiapine	116 (9.7)
		Aripiprazole	95 (7.9)
		Olanzapine	84 (7.0)
		Paliperidone	69 (5.8)
		Clozapine	38 (3.2)

[a]The number of patients with CGI-S data was n=887.

Figure 3. Rehospitalization Rate Within 12 Months



Treatment group	Day 30	Day 365	Median time to rehospitalization	Log-rank
LAI only (n=156)	21%	69%	210 days	0.03
LAI+OA (n=183)	37%	74%	96 days	
Overall (n=339)	30%	72%	135 days	-

HR in rehospitalization model was adjusted for pre-healthcare resource utilization, region, and index hospitalization length of stay.

Table 4. Comparison of First Treatment Path (LAI Continuation Compared to Treatment Discontinuation) Post-Discharge by LAI Dosing Interval

	Index LAI Dosing		
n (%)	Dosed once monthly or less n=271	Dosed more often than once monthly n=178	*P* value
Treatment path: patient continued with index LAI	38 (14.0)	8 (4.5)	<.01
At 3 months	101 (37.3)	28 (15.7)	<.01
At 6 months	62 (22.9)	13 (7.3)	<.01
At 12 months	38 (14.0)	8 (4.5)	<.01
Patient continued with index LAI and co-prescribed OA post-discharge	13 (34.2)	4 (50.0)	.66
Treatment path: patient discontinued all treatment	204 (75.3)	154 (86.5)	.01
No treatment at 3 months	166 (61.3)	143 (80.3)	<.01
at 6 months	191 (70.5)	152 (85.4)	<.01
at 12 months	204 (75.3)	154 (86.5)	.01
Patient restarted index LAI after discontinuation	81 (39.7)	68 (44.2)	.46

Conclusions

- **Prior to LAI initiation, the most prescribed OA was risperidone. Although the American Psychiatric Association suggests patients with symptom improvement with an OA continue the same antipsychotic as an LAI, the most prescribed LAI was haloperidol during hospitalization, followed by risperidone q2w**
- **OAs were often prescribed with LAIs, without showing benefit in rehospitalization rate/risk or outpatient visits**
- **Patients taking LAIs dosed once monthly or less often had better adherence and persistence post-discharge than those prescribed LAIs dosed more often**

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Abbreviations
– not applicable, CGI-S = Clinical Global Impression-Severity, DB = database, EHR = electronic health record, HR = hazard ratio, ICD = International Classification of Diseases, IQR = interquartile range, IRR = incidence rate ratio; LAI = long-acting antipsychotic agent, OA = oral antipsychotic agent, q1m = dosed once monthly, q2m = dosed once every two months, q2w = dosed once every two weeks, q4w = dosed once every 4 weeks, q6w = dosed once every 6 weeks, US = United States

References
1. Buckley PF, et al. *Schizophr Bull*. 2009;35:383–402.
2. Subotnik KL, et al. *JAMA Psych*. 2015;72:822–829.
3. Greene M, et al. *J Med Econ*. 2018;21:127–134.