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ORIGINAL RESEARCH

Treatment Patterns and Outcomes from OASIS: A Prospective Observational Study of Long-Acting Injectables in Schizophrenia

Peter J Weiden[1], Lauren N Strand[2], Michael J Doane[2], Christina Arevalo[2], James A McGrory[2], Eric D Achtyes[3], Philip D Harvey[4], John M Kane[5], Stephen R Saklad[6], Jeffrey Trotter[7,8], Dawn I Velligan[9]

[1]Renaissance School of Medicine at Stony Brook University, Stony Brook, NY, USA; [2]Alkermes, Inc., Waltham, MA, USA; [3]Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI, USA; [4]University of Miami Miller School of Medicine, Miami, FL, USA; [5]The Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA; [6]College of Pharmacy, Division of Pharmacotherapy, The University of Texas at Austin, UT Health Science Center San Antonio, San Antonio, TX, USA; [7]Worldwide Clinical Trials, Research Triangle Park, Durham, NC, USA; [8]J Trotter Research & Consulting, Highland Park, IL, USA; [9]UT Health Science Center San Antonio, San Antonio, TX, USA

Correspondence: Michael J Doane, Alkermes, Inc., 900 Winter Street, Waltham, MA, 02451, USA, Tel +1 781 609 6364, Email Michael.Doane@alkermes.com

Purpose: OASIS (NCT03919994) was a prospective, observational study designed to provide insights on real-world outcomes associated with atypical long-acting injectable (LAI) antipsychotic medications.

Patients and Methods: OASIS (March 2019–January 2023) was conducted across 63 US sites. Adults (≥18 years) with schizophrenia who newly initiated one of four atypical LAI antipsychotics (aripiprazole lauroxil, aripiprazole monohydrate, paliperidone palmitate, or risperidone long-acting injection [microsphere formulation]) were enrolled and followed for up to 12 months in routine care. Treatment patterns (reasons for treatment initiation, duration of use, rates of switching/discontinuation) were assessed. Outcomes included Clinical Global Impression–Severity (CGI-S), Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS) scale, and patient-reported Glasgow Antipsychotic Side-Effect Scale (GASS) scores. Results are summarized descriptively.

Results: Overall, 277 patients with schizophrenia enrolled and received ≥1 injection. Most common reasons for initiating atypical LAI antipsychotics at baseline were the presence of persistent psychotic symptoms (50%) and adherence challenges with oral antipsychotics (44%). Mean (SD) time on index treatment was 210.0 (145.3) days. Overall, 130 (47%) patients completed 12 months of follow-up; 74% of them remained on the treatment initiated until the end of study participation. Most study visits were conducted in person and were planned/scheduled versus crisis visits. Mean (SD) baseline CGI-S score was 4.2 (1.1), indicating moderate illness severity; individual CRDPSS symptom scores were mild (mean [SD] delusions score, 2.0 [1.4]; hallucinations, 1.9 [1.4]; negative symptoms, 1.6 [1.3]) at baseline and remained stable after treatment initiation. Antipsychotic side effects were generally absent or mild at baseline (mean [SD] GASS total score, 10.7 [10.3]) and over follow-up.

Conclusion: Treatment patterns in this observational study reinforced the real-world utility of atypical LAI antipsychotics in the treatment of schizophrenia. Results suggest that patients initiating treatment remained clinically stable with mostly absent or mild side effects for up to 12 months of follow-up.

Plain Language Summary: Atypical long-acting injectable (LAI) antipsychotic medications may be underused in the treatment of schizophrenia. In the Observational Study of Long-Acting Injectables in Schizophrenia (OASIS) study, we wanted to better understand the benefits of these medications in the real world. We followed patients with schizophrenia who started taking one of four atypical LAI antipsychotics: aripiprazole lauroxil, aripiprazole monohydrate, paliperidone palmitate, or risperidone. We looked at patterns of how clinicians and patients used these medications and how patients benefited from treatment for up to 1 year. All patients were treated according to their clinician's practice of routine care; the recommendation to start treatment and the medication chosen were up to the patients and their clinician. Most patients in the study were treated at a community mental health clinic or private practice, not a hospital. Illness severity was moderate and symptoms were mild at the start of the study. After they started taking an atypical LAI antipsychotic, most patients stayed on the medication that they started. Only a few patients switched to a different medication or stopped taking medication altogether. Despite the COVID-19 pandemic, most healthcare visits were in person and were planned rather

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than crisis visits. Over the course of up to 1 year of follow-up, illness severity and symptoms were stable, and most patients experienced no or mild side effects from the medication they were taking. These results show the utility of atypical LAI antipsychotic medications for the treatment of patients with schizophrenia in a real-world setting.

Keywords: antipsychotic, aripiprazole, paliperidone palmitate, patient-reported outcome measures, risperidone

Introduction

Antipsychotic medications are recommended as first-line treatment for schizophrenia because of their effectiveness in controlling the symptoms of the disease.[1,2] When taken as prescribed, antipsychotic medications are associated with a reduced risk of symptom relapse[3–5] and potential improvement in functional and quality-of-life outcomes.[6,7] However, suboptimal adherence is a common obstacle to successful treatment in some patients with schizophrenia.[8–10]

Long-acting injectable (LAI) formulations of antipsychotic medications were developed to address challenges with treatment adherence.[11] They are designed to deliver therapeutic levels of drug over an extended period of time, from weeks to months, which may be useful in overcoming suboptimal adherence and improving quality of life in patients with schizophrenia.[12,13] Several atypical LAI antipsychotic medications are approved by the US Food and Drug Administration and are available for use in patients with schizophrenia.[14] Therefore, patients and clinicians have a range of treatment options from which to choose, and they all differ with respect to their active molecule, dosing regimen and frequency, side-effect profile, and initiation regimen.[12]

Evidence suggests that available LAI antipsychotics have broadly comparable clinical efficacies among them and that their use is associated with reduced rates of relapse and hospitalization.[15–20] Despite conferring therapeutic advantages, LAI formulations of antipsychotics are underused, particularly in the United States.[11,21] Although estimates vary by methodology, some studies have reported use rates of about 5% to 20% in eligible patients with schizophrenia.[22–24] This underuse gives rise to gaps in our understanding of the role that LAI antipsychotics play in the treatment of schizophrenia, especially in real-world clinical settings.

Observational research designs facilitate studying treatment outcomes that are relevant to everyday clinical practice.[25] They can capture the natural course of treatment and the practical considerations that patients and clinicians face during treatment, identify treatment patterns, and assess the long-term effectiveness and safety of interventions.[11,25,26] Observational studies can also provide information on patient populations and subgroups that may be underrepresented in randomized controlled trials (RCTs).[25,26] Thus, insights derived from observational studies complement those from RCTs, which offer a more standardized environment for treatment delivery and outcome assessment.[15,25] However, to date, there have been few observational studies that prospectively evaluated the outcomes associated with atypical LAI antipsychotic use.

The Observational Study of Long-Acting Injectables in Schizophrenia (OASIS; NCT03919994) was a prospective observational study that sought to provide comprehensive data on real-world outcomes associated with atypical LAI antipsychotic use for the treatment of schizophrenia. The objectives of OASIS were to examine the baseline demographic, clinical, and socioeconomic characteristics of patients with schizophrenia who started one of four US Food and Drug Administration–approved atypical LAI antipsychotics; the associated treatment patterns observed over a period of up to 12 months of follow-up; and clinician- and patient-reported outcomes over that follow-up period.

Materials and Methods

Study Design and Treatment

OASIS was a prospective, noninterventional, multicenter cohort study conducted from March 2019 to January 2023 to assess the real-world experiences of adult patients with schizophrenia who were initiated on intramuscular (IM) injections of one of four atypical LAI antipsychotics: aripiprazole lauroxil, aripiprazole monohydrate, paliperidone palmitate, or risperidone. Index atypical LAI antipsychotic initiation occurred in the 10 days before to 30 days after the baseline visit (study day 1).

The initial target enrollment for OASIS was 1000 patients with schizophrenia who were being treated in community-based outpatient sites. The first patient was enrolled in June 2019. In January 2020, the protocol was amended to include sites that initiated atypical LAI antipsychotics in inpatient settings as well. The conduct of the study coincided with the COVID-19 pandemic, leading to challenges with patient enrollment. In the fourth quarter of 2021, the study sponsor made the decision to stop patient enrollment and follow the 339 patients who were enrolled at that time.

This study was conducted in accordance with the ethical principles derived from the Declaration of Helsinki and with all legal and regulatory requirements. The study followed the International Society for Pharmacoepidemiology's guidelines for good pharmacoepidemiology practice,[27] the International Epidemiological Association's guidelines for good epidemiological practice,[28] the International Society for Pharmacoeconomics and Outcomes Research's good research practices,[29] the Council for International Organizations of Medical Sciences' international ethical guidelines for epidemiological studies,[30] and the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance's guide on methodological standards in pharmacoepidemiology.[31] The protocol and all amendments were approved by an institutional review board or ethics committee at each study site. All patients provided written informed consent before participating in any study-specific procedures.

Study Population

Key Inclusion and Exclusion Criteria

Adults aged ≥18 years with a clinician's diagnosis of schizophrenia were eligible. Eligible patients had been seen by the treating clinician at least once within the 12 months before study enrollment and had not received treatment with any atypical LAI antipsychotic in the 6 months before the baseline visit. Information on the use of typical LAI antipsychotics in the 6 months before the baseline visit was not collected. Patients were ineligible if they were currently participating or planning participation in an interventional clinical study or had participated in an interventional clinical study within 30 days before enrollment. Patients were also excluded if, in the opinion of the investigator, they were considered an imminent danger to themselves; a prior history of suicidal ideation or suicidal attempt was not exclusionary.

Study Visits

Patients were enrolled after their clinician's decision to initiate an atypical LAI antipsychotic in either an inpatient or outpatient setting. The clinician directed all aspects of treatment, including any required procedures, and determined the frequency of follow-up visits. Patients were followed for up to 12 months. Patients who discontinued treatment were asked to remain in the study for the full follow-up duration; however, patients could end their participation at any time.

Baseline Demographic, Location-of-Care, and Clinical Characteristics

Baseline demographic information, including age, sex, race, insurance status, living situation, and challenges accessing outpatient care, was recorded. Baseline clinical characteristics included illness severity, time since receiving a diagnosis of schizophrenia, and comorbid mental health–related conditions. Location-of-care characteristics, including the US region and setting type in which care was received, were recorded. Antipsychotic use in the 12 months before baseline was assessed, as was whether the index atypical LAI antipsychotic was initiated on an inpatient or outpatient basis. Healthcare resource use, based on available medical records or patient report, was also assessed in the 12 months before baseline.

Treatment Patterns

Treatment patterns were evaluated prospectively for up to 12 months following the baseline visit. The types of healthcare visits that occurred during the study were recorded. Visits were categorized by whether they were in-person/on-site or virtual and by whether they were planned (routine) or crisis visits. Also captured were the reasons for initiating treatment with an atypical LAI antipsychotic. Likewise, reasons for choosing a specific atypical LAI antipsychotic agent (either for treatment initiation or when switching treatments) were documented. Key outcomes included the duration of index LAI antipsychotic use and the rates of switching and discontinuing treatment.

Clinician- and Patient-Reported Outcomes

Illness severity was assessed using the Clinical Global Impression–Severity (CGI-S) scale, a clinician-rated assessment of mental illness severity scored on a scale of 1 (normal, not at all ill) to 7 (most extremely ill).[32] The severity of the individual symptoms of schizophrenia was evaluated using the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS) scale.[33] The DSM-5 CRDPSS is an 8-item measure used to capture the severity of psychosis symptom dimensions, including hallucinations, delusions, disorganized speech, abnormal psychomotor behavior, negative symptoms, impaired cognition, depression, and mania, all scored on a scale of 0 (not present) to 4 (present and severe). Patient-reported outcomes included the Glasgow Antipsychotic Side-Effect Scale (GASS), a measure with 22 questions assessing antipsychotic medication side effects (eg, My legs have felt restless and/or I could not sit still [ie, akathisia]) and scored on a scale of 0 (never) to 3 (everyday).[34]

Statistical Analysis

Due to the descriptive nature of the study, no formal sample size was calculated. All outcomes were analyzed using descriptive statistics; no inferential analysis was conducted. Follow-up windows approximating 1-month increments were used to measure changes from baseline at comparable timepoints across patients. Some patients may have missed a visit during one of their follow-up windows. Patients in those cases did not have follow-up data during that interval but remained in the study and were further observed over the 12-month follow-up period or until they discontinued from the study. Missing data were not imputed.

Summary statistics (means [SD], numbers, and proportions) were generated for baseline demographics and location-of-care and clinical characteristics. Treatment patterns associated with atypical LAI antipsychotic use were summarized as means (SD), medians, numbers, and proportions. Illness severity (CGI-S), symptom severity (CRDPSS), and patient-reported side effects of antipsychotic medications (GASS) were summarized as mean (SD) change from baseline. Data were pooled across all atypical LAI antipsychotics and are presented in aggregate. Additional information categorized by individual atypical LAI antipsychotic is presented in the supplementary materials, except for risperidone long-acting injection, which is not reported separately because of the low number of patients initiated on this agent. Because OASIS was observational and patients were not randomly assigned to treatment, no statistical comparisons were made across the different atypical LAI antipsychotics studied.

Results

Baseline Demographic, Location-of-Care, and Clinical Characteristics

A total of 339 patients with schizophrenia were enrolled in OASIS (Figure 1). Of these, 62 were excluded for several reasons, including not meeting the inclusion/exclusion criteria or being incorrectly enrolled, and followed by the study site. Overall, 277 patients with schizophrenia received ≥1 injection and were included in the analysis, with 96 initiating aripiprazole lauroxil, 61 initiating aripiprazole monohydrate, 111 initiating paliperidone palmitate, and 9 initiating risperidone long-acting injection. Most patients were male (66%), White (47%), unemployed (53%), and insured by Medicaid or Medicare (47% and 30%, respectively) (Table 1 and Supplementary Table 1). Baseline severity of illness was moderate, with a mean (SD) CGI-S score of 4.2 (1.1) (Table 1 and Supplementary Table 1). Comorbid anxiety (25%), depression (24%), and a history of substance use disorder (44%) were common among patients. Enrolled patients came primarily from the southern United States (51%) and from an urban care (61%) community mental health clinic (46%) or private practice (45%) (Table 2 and Supplementary Table 2). In the 12 months before the baseline visit, 21% of patients had ≥1 schizophrenia-related emergency department visit, 63% had ≥1 schizophrenia-related outpatient visit (Table 3 and Supplementary Table 3), and 35% had used an antipsychotic (Table 3 and Supplementary Table 3). Most patients (64%) initiated their respective atypical LAI antipsychotic in an outpatient setting.

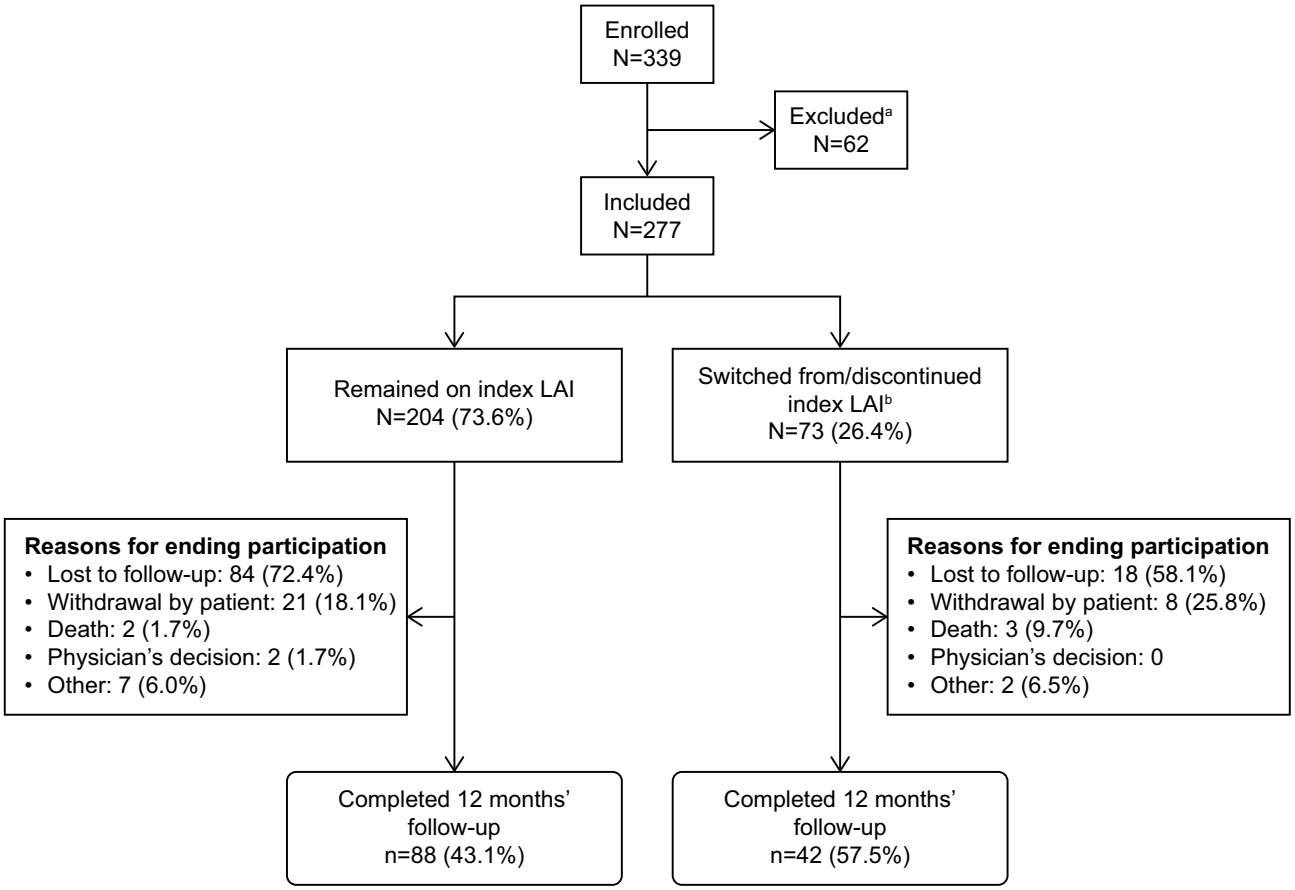

Figure 1 Patient Disposition. [a]Includes patients who did not meet inclusion/exclusion criteria or were incorrectly enrolled. [b]Includes patients who switched to an oral antipsychotic, switched to another atypical LAI antipsychotic, and those who discontinued treatment altogether.
Abbreviation: LAI, long-acting injectable.

Study Disposition and Treatment Patterns

In total, 63 study sites in the United States participated in OASIS; 44 sites enrolled at least 1 patient, and 42 sites contributed data to the study. Although no study visits were mandated, patients were seen by their clinician approximately every month. Overall, 47% of patients who were enrolled in OASIS completed the full 12 months of follow-up (Figure 2). The mean (SD) time in the study was 249.3 (146.7) days (about 8 months), with a median of 329.0 days (about 11 months). The most common reasons for patients ending participation were loss to follow-up (69%) and patient decision (20%).

Table 1 Baseline Demographic and Clinical Characteristics

Characteristic	Total (N=277)
Age, mean (SD), years	37.7 (14.9)
Male, n (%)	182 (65.7)
White, n (%)	131 (47.3)
Unemployed, n (%)	147 (53.1)

(*Continued*)

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Table 1 (Continued).

Characteristic	Total (N=277)
Insurance status,[a,b,c] n (%)	
Uninsured	37 (13.4)
Insured	231 (83.4)
Medicaid	130 (46.9)
Medicare	84 (30.3)
Private insurance	40 (14.4)
Single, never married, n (%)	209 (75.5)
Lives with family, n (%)	149 (53.8)
Reported challenges accessing outpatient care, n (%)	99 (35.7)
Reason for challenges,[c] n (%)	
Travel to site	60 (60.6)
Help needed to get to visit	54 (54.5)
Payment for visit	18 (18.2)
Other[d]	17 (17.2)
CGI-S score,[e] mean (SD)	4.2 (1.1)
Time since schizophrenia diagnosis,[f] mean (SD), years	11.9 (12.5)
Comorbid mental health–related conditions,[g] n (%)	
History of substance use disorder,[h] n (%)	121 (43.7)
Anxiety	70 (25.3)
Depression	66 (23.8)

Notes: [a]Unknown/not reported, missing response, and other (n=33). [b]Includes responses such as the Affordable Care Act (n=11) or similar programs. [c]Multiple responses allowed. [d]Includes childcare difficulties, getting medication approved, medication delivery delays, and other travel issues. [e]Score of 4 corresponds to "moderately ill", and a score of 3 corresponds to "mildly ill". [f]Available for 230 patients. [g]Ongoing at baseline. [h]Includes alcohol, marijuana, methamphetamine, stimulant, opioid, and other use disorders.

Abbreviation: CGI-S, Clinical Global Impression–Severity.

Table 2 Location-of-Care Characteristics

Characteristic	Total (N=277)
Region, n (%)	
South	142 (51.3)
West	61 (22.0)
Midwest	45 (16.2)
Northeast	29 (10.5)

(*Continued*)

Table 2 (Continued).

Characteristic	Total (N=277)
Type of site,[a,b,c] n (%)	
Community mental health clinic	128 (46.2)
Independent or private practice	125 (45.1)
Academic center	15 (5.4)
Hospital network	29 (10.5)
Other	9 (3.2)
Site location type,[c] n (%)	
Urban	168 (60.6)
Suburban	83 (30.0)
Rural	12 (4.3)

Notes: [a]Multiple responses allowed. [b]The study protocol was amended to include locations of care that treated inpatients who initiated an atypical LAI antipsychotic. [c]Not reported (n=14).
Abbreviation: LAI, long-acting injectable.

Table 3 Healthcare Resource Use,[a] Antipsychotic Use,[a] and Atypical LAI Administration Setting

Characteristic	Total (N=277)
≥1 schizophrenia-related ED visit, n (%)	57 (20.6)
ED visits per patient, mean (SD)	1.4 (0.7)
≥1 schizophrenia-related inpatient visit, n (%)	111 (40.1)
Inpatient visits per patient, mean (SD)	1.4 (0.7)
Length of inpatient stay, mean (SD), days	15.2 (28.4)
≥1 schizophrenia-related outpatient visit, n (%)	175 (63.2)
Outpatient visits per patient, mean (SD)	9.1 (26.5)
Antipsychotic use in the prior 12 months,[b] n (%)	96 (34.7)
Atypical LAI antipsychotics, n (%)	7 (7.3)
Oral antipsychotics, n (%)	93 (96.9)
Setting of first atypical LAI antipsychotic administration, n (%)	
Outpatient	177 (63.9)
Inpatient	33 (11.9)
Board and care	7 (2.5)
Other	3 (1.1)
Missing	57 (20.6)

Notes: [a]In the 12 months before baseline. [b]Summarized from medical history and concomitant medication data, based on a combination of patient records and self-report; observed rates may underestimate actual rates.
Abbreviations: ED, emergency department; LAI, long-acting injectable.

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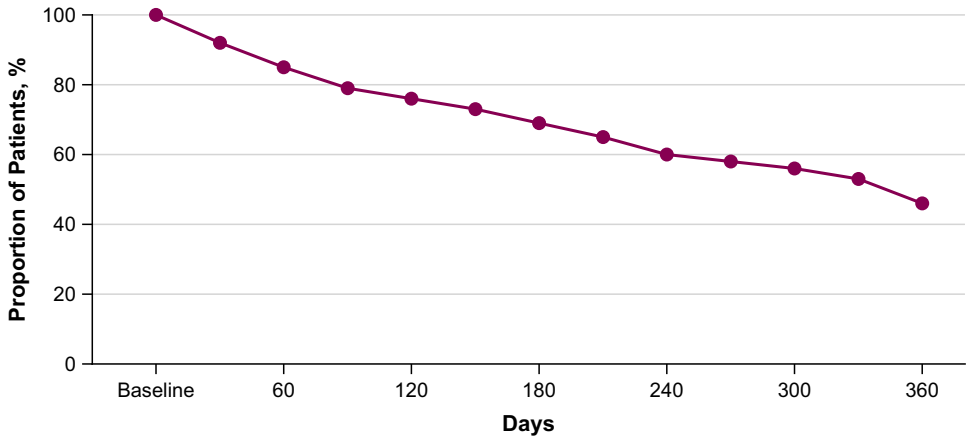

Figure 2 Study Attrition.

The most common reasons that clinicians decided to initiate atypical LAI antipsychotic treatment were the presence of persistent psychotic symptoms (50%), the need for better clinical monitoring due to suboptimal adherence (44%), and patient request (26%) (Table 4 and Supplementary Table 4). The most common reasons for selecting a specific atypical LAI antipsychotic were the clinician's experience with that medication over others (40%), a history of efficacy with the oral equivalent (36%), and the patient's preference for a specific injection interval (16%) (Table 4 and Supplementary Table 4).

The mean (SD) time on the index atypical LAI antipsychotic initiated was 210.0 (145.3) days (7 months), with a median of 200.0 days (about 7 months). Nearly 74% of patients remained on the index atypical LAI antipsychotic medication that was initiated for the entire time that they were enrolled in the study (Figure 3). Overall, 26% of patients stopped their index medication and switched to an oral antipsychotic (9%), switched to another atypical LAI antipsychotic (9%), or discontinued treatment altogether (8%). Questions related to the reasons for switching or discontinuing the index medication were provided by only a few clinicians for 6% to 12% of patients. The most common reasons for stopping the index medication were patient decision against advice (33%) and wanting to achieve a better therapeutic effect (19%).

Table 4 Reported Reasons for Initiating Atypical LAI Antipsychotics

	Total (N=277)
Reasons for initiating any LAI antipsychotic,[a] n (%)	
Persistent psychotic symptoms	139 (50.2)
Need for better monitoring due to suboptimal adherence	123 (44.4)
Patient request	72 (26.0)
Family request	38 (13.7)
History of improvement on atypical LAI antipsychotics	37 (13.4)
Recommended by case manager or another clinician	34 (12.3)
Persistent psychotic symptoms in setting of substance abuse problems	22 (7.9)
Recent or anticipated change in living situation	19 (6.9)
Other	14 (5.1)

(*Continued*)

Table 4 (Continued).

	Total (N=277)
Reasons for selecting a specific atypical LAI antipsychotic,[a] n (%)	
Clinician's experience with a specific atypical LAI over others	112 (40.4)
Efficacy history with oral version	101 (36.5)
Patient's preference for injection interval	44 (15.9)
Tolerability history	41 (14.8)
Patient's history of efficacy or tolerability problems with another medication	35 (12.6)
Easily accessible	17 (6.1)
Clinician's experience with oral equivalent over others	14 (5.1)
Clinician's preference for dosing options	9 (3.2)
Other	30 (10.8)

Note: [a]Multiple responses allowed; therefore, responses may not sum to 100%.
Abbreviation: LAI, long-acting injectable.

Study Visits

Although the majority of healthcare visits in this study occurred after the COVID-19 pandemic began, most visits were conducted in person/on site (mean [SD] per person: 4.5 [4.3]) versus virtually (mean [SD] per person: 0.8 [1.6]) (Figure 4). Study visits were primarily planned/scheduled (mean [SD] number of planned visits per person: 5.6 [4.6]) versus crisis visits (0.1 [0.4]).

Clinician- and Patient-Reported Outcomes

Illness severity, as assessed by the CGI-S, was moderate at baseline, with a mean (SD) of 4.2 (1.1). At the end of the follow-up period, mean (SD) change in CGI-S score was –0.7 (1.1) points among patients with available data (Figure 5). Mean individual symptom scores at baseline ranged from equivocal to mild, as assessed on the DSM-5 CRDPSS scale. Psychotic symptoms remained stable with atypical LAI treatment across most domains in observed cases (Figure 6A–G). Patient-reported side effects of antipsychotic medications were absent or mild at baseline, with a mean (SD) GASS score of 10.7 (10.3). During follow-up, patient-reported antipsychotic medication side effects remained absent or mild with

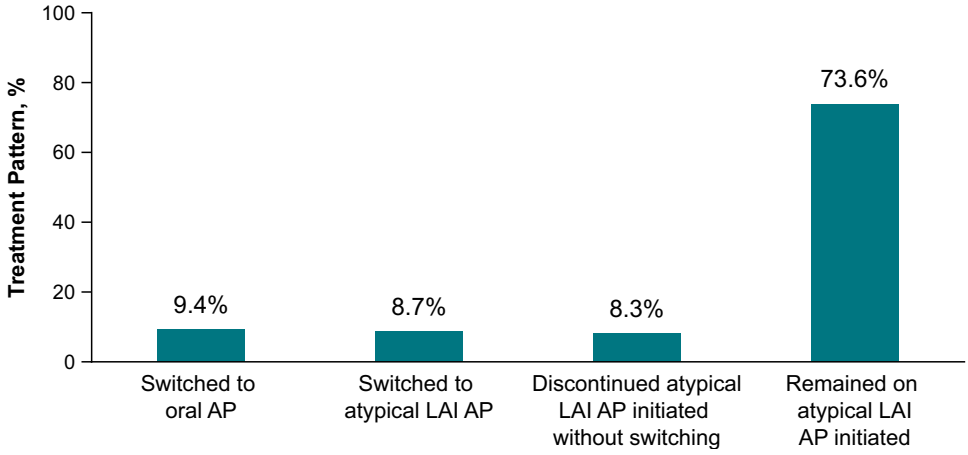

Figure 3 Treatment Patterns. Data do not account for patients who stopped the study before 12 months. Data were derived from concomitant medication reporting.
Abbreviations: AP, antipsychotic; LAI, long-acting injectable.

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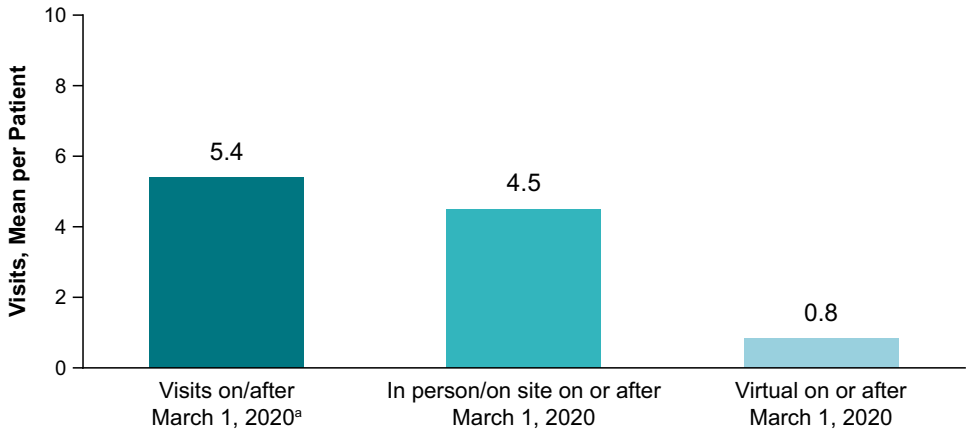

Figure 4 Visit Patterns During the COVID-19 Pandemic (N=277). [a]Approximate start of the COVID-19 pandemic.
Abbreviation: COVID-19, coronavirus disease 2019.

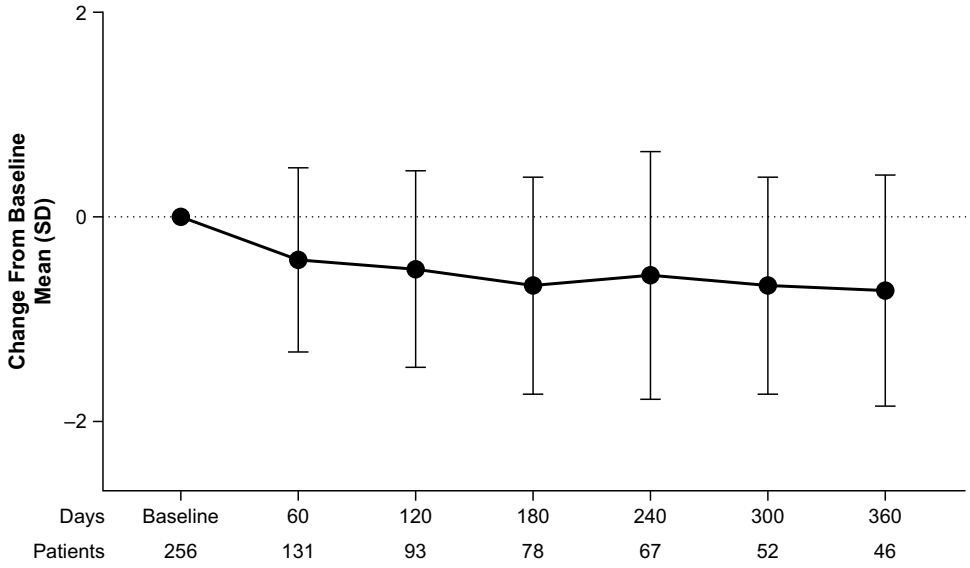

Figure 5 Illness Severity as Assessed by CGI-S Scores (Observed Cases). No statistical comparisons were conducted.
Abbreviation: CGI-S, Clinical Global Impression–Severity.

atypical LAI antipsychotic treatment (Figure 7). Each atypical LAI antipsychotic treatment cohort had similar changes over time across illness severity, symptom severity, and side effects experienced.

Discussion

The results from OASIS provide real-world data on patients with schizophrenia who initiated one of four atypical LAI antipsychotics. Patients who enrolled in the study received care primarily in an outpatient community mental health clinic or private practice. At enrollment, illness severity was moderate, although approximately one-third of treated patients had taken antipsychotic agents in the previous 12 months. During the study, approximately one-fifth of the patients switched their treatment to either another atypical LAI antipsychotic medication or an oral antipsychotic medication; fewer than 10% of the patients discontinued antipsychotic treatment entirely. Among patients with available data who were enrolled in OASIS, illness severity and symptoms of schizophrenia remained stable with atypical LAI antipsychotic treatment during the follow-up period. By patient report, side effects associated with atypical LAI antipsychotic treatment were absent or mild during the study, similar to the side-effect burden reported at baseline before atypical LAI antipsychotic

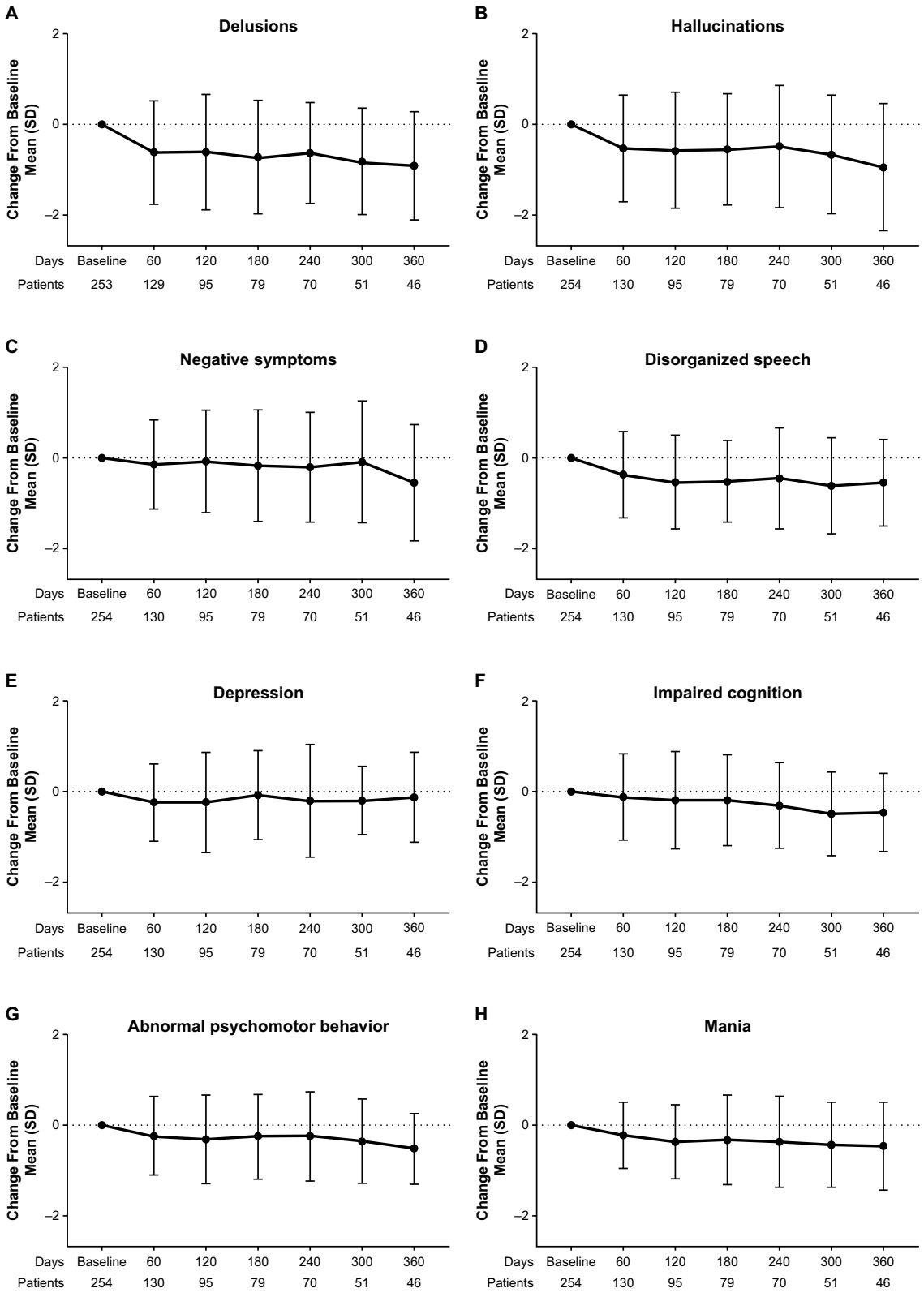

Figure 6 Symptom Severity as Assessed by CRDPSS Scores (Observed Cases): Changes From Baseline in Delusions (**A**), Hallucinations (**B**), Negative Symptoms (**C**), Disorganized Speech (**D**), Depression (**E**), Impaired Cognition (**F**), Abnormal Psychomotor Behavior (**G**), and Mania (**H**). No statistical comparisons were conducted.
Abbreviation: CRDPSS, Clinical-Rated Dimensions of Psychosis Symptom Severity.

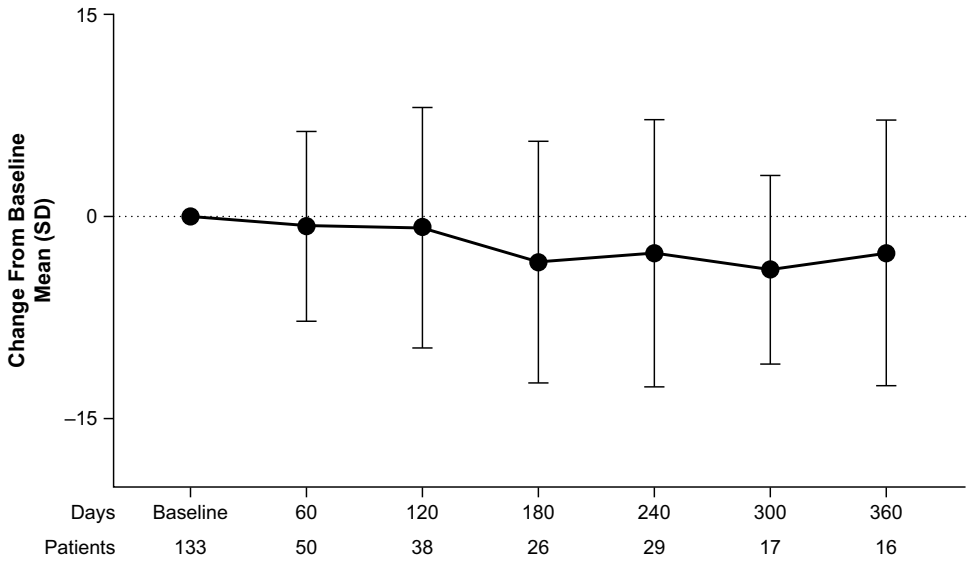

Figure 7 Side Effects of Antipsychotics as Assessed by GASS Scores (Observed Cases). Total GASS score (0–66) can be interpreted continuously or as 0–21=absent or mild, 22–42=moderate, ≥43=severe. No statistical comparisons were conducted.
Abbreviation: GASS, Glasgow Antipsychotic Side-Effect Scale.

initiation. Because side effects were assessed via patient reporting, they may differ from clinician-reported side effects as assessed in other studies.

Despite the challenges of the COVID-19 pandemic, most study visits occurred in person, and almost half of the enrolled patients completed the full 12 months of follow-up, with nearly three-quarters remaining on the atypical LAI antipsychotic they initiated for the entire time they participated in the study. The high proportion of in-person study visits is notable given the governmental guidelines during the COVID-19 pandemic regarding travel and social distancing and suggests that patients who enrolled in OASIS maintained their normal course of care. This finding is consistent with the results reported in OASIS-MAPS, an observational online survey that was a part of OASIS focusing on the impact of the COVID-19 pandemic on the management of schizophrenia with LAI antipsychotic formulations.[35] In that analysis, the 35 treatment sites that were surveyed adapted to the pandemic to continue to provide care for patients. While most reported adopting or expanding telepsychiatry services, some sites also adopted measures to continue in-person care and improve medication adherence that included educating patients on how to reduce their risk of COVID-19 exposure when leaving their homes, providing alternative sites to administer LAI antipsychotic medications, and assisting with transportation to appointments.[35] These adjustments to the continuum of care during the COVID-19 pandemic may explain in part the high proportions of in-person study visits observed in OASIS. Also notable were the low proportions of patients who discontinued atypical LAI antipsychotic treatment entirely. Most sites participating in the OASIS-MAPS survey also reported a minimal impact of the pandemic on observed adherence,[35] consistent with results from OASIS and other studies of LAI antipsychotic medication use in patients with schizophrenia during the pandemic.[36–38]

These results also align more broadly with those of previous clinical and observational studies in which atypical LAI antipsychotic medications were effective treatments for schizophrenia with side-effect profiles that resembled those of their oral counterparts.[15,39–43] Although side-effect data in OASIS were collected via patient self-report, the findings are in agreement with data obtained using more standardized collection procedures, such as those conducted in RCTs, in which side effects stabilized during antipsychotic treatment.[42,44,45]

For patients with schizophrenia who have factors that complicate treatment such as suboptimal medication adherence or substance use, LAI antipsychotic formulations may provide a way to decrease healthcare burden while improving quality of life.[13,46] However, these medications may also be a valuable option for patients early in their illness, in whom early initiation of treatment with LAI antipsychotic medication has been shown to improve clinical outcomes.[15,47] In previous observational studies, the use of LAI antipsychotic formulations for schizophrenia was associated with

reductions in healthcare resource utilization.[23,48,49] Although OASIS did not evaluate measures of functioning, improvements in quality of life have been observed following treatment with LAI antipsychotic medications.[13,50] Along with nearly three-quarters of the patients remaining on their index medication, the stability of illness severity and the absence or mildness of side effects suggest that atypical LAI antipsychotic medications have good long-term tolerability and the potential for sustained clinical effectiveness in managing the symptoms of schizophrenia. The OASIS findings also suggest that clinicians may consider the use of atypical LAI antipsychotic formulations as a feasible treatment strategy during periods of instability, such as with the COVID-19 pandemic, while future research should prioritize long-term evaluations of quality of life and functional outcomes to guide more personalized care.

Strengths and Limitations

Prospective, observational cohort studies with repeated assessments, such as OASIS, are uncommon yet valuable for understanding the real-world role of atypical LAI antipsychotic medications in the treatment of schizophrenia. In contrast to RCTs, where patients generally receive a more regimented level of care than is routinely available in a clinical practice setting (frequent visits, rapid dose titrations, intensive assessments, and perhaps other psychosocial assistance and services),[11,15] the observed treatment patterns and outcomes reported here reflect clinical scenarios and standards of care that are more generalizable to the broader population of patients living with schizophrenia and are reflective of the variables that are considered when initiating atypical LAI antipsychotics.

Limitations of OASIS should be noted. A key limitation is the absence of inferential statistical analyses. Although the primary objective was to provide a descriptive overview of atypical LAI antipsychotic medication use in a real-world setting, modern observational research often incorporates comparative or regression-based methods to identify associations and adjust for potential confounders. The OASIS dataset includes several clinically relevant dimensions, such as substance use history, recent hospitalization, and specific medications initiated, that could support subgroup analyses and more rigorous statistical modeling. These variables were not explored analytically in the current study due to sample-size constraints, but they have potential value as important targets for future research using more advanced analytic approaches. OASIS was designed to prioritize a noninterventional observational approach, to optimize data collection, and to facilitate clinician and patient engagement. Comprehensive assessments of disease symptoms or side effects of antipsychotic medications were not conducted. Furthermore, quality-of-life or other measures of functioning were not assessed, and information on typical LAI use in the 12 months before baseline was not available. The overall sample size was lower than planned, in part due to challenges associated with the COVID-19 pandemic, which limited the ability to completely describe outcomes in individual atypical LAI antipsychotic medications and to draw meaningful conclusions from any observed differences. Likewise, the low enrollment of patients initiating risperidone long-acting injection may not reflect actual patterns of use. The baseline characteristics and outcomes observed among patients may not be fully generalizable to the larger population of people living with schizophrenia who are treated with an atypical LAI antipsychotic. Some patients were lost to follow-up and/or did not contribute complete data. The study did not include data on older typical LAI antipsychotics (eg, haloperidol decanoate, fluphenazine decanoate) or other atypical LAI antipsychotic medications that became available during or after the study period. The study goal was to capture real-world clinician and patient decisions made regarding atypical LAI antipsychotic choice; however, the possibility that participation in this research study affected treatment decisions cannot be excluded.

Conclusion

The results from OASIS help to fill gaps in real-world research on atypical LAI antipsychotic use in patients with schizophrenia. The outcomes observed herein highlight the feasibility and utility of atypical LAI antipsychotic use in the ongoing treatment of patients with schizophrenia, even during periods of hardship, such as with the COVID-19 pandemic. Given the descriptive nature of the analysis, the absence of statistical testing, and the lack of functional outcome measures, these results should be interpreted with caution. They are not intended to be generalized to all individuals with schizophrenia or used to inform policy decisions without further validation. Future research should aim to include more analytically rigorous approaches, explore patient subgroups and characteristics that may influence

treatment response, and consider longer-term outcomes—potentially through technology-assisted methods such as collecting data from wearables—to enhance the depth and applicability of findings.

Previous Presentations

Interim findings of this study were presented as a poster presentation at the US Psych Congress, September 6–10, 2023, Nashville, TN; NEI Fall Congress, November 9–12, 2023, Colorado Springs, CO; AMCP Annual Meeting, April 16–19, 2024, New Orleans, LA; and AAPP Annual Meeting, April 7–10, 2024, Orlando, FL. The poster's abstract was published in "Poster Abstracts" in *J Manag Care Spec Pharm* 2024;30(4-a Suppl):S1-S135: https://doi.org/10.18553/jmcp.2024.30.4-a.s1; and in "AAPP 2024 Annual Meeting Poster Abstracts" in *Ment Health Clin* 2024;14(2):111-194: https://doi.org/10.9740/mhc.2024.04.111.

Abbreviations

CGI-S, Clinical Global Impression–Severity; CRDPSS, Clinician-Rated Dimensions of Psychosis Symptom Severity; DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; GASS, Glasgow Antipsychotic Side-Effect Scale; IM, intramuscular; LAI, long-acting injectable; OASIS, Observational Study of Long-Acting Injectables in Schizophrenia; RCT, randomized controlled trial.

Data Sharing Statement

The data collected in this study are proprietary to Alkermes, Inc. Alkermes, Inc. is committed to public sharing of data in accordance with applicable regulations and laws, and requests can be submitted to the corresponding author.

Ethics Approval and Informed Consent

All participants provided informed consent. The investigator at each study site documented institutional review board (IRB) approval for the study protocol and any amendments, informed consent forms and revisions, patient recruitment documents, and any other study documentation provided to patients. This study was approved by the following IRBs: Georgia Department of Public Health IRB/Augusta, Jamaica Hospital Medical Center IRB, Partners Human Research System IRB, PeaceHealth System IRB, Springfield Committee for Research Involving Human Subjects IRB, State of New Hampshire Department of Health and Human Services IRB, Sterling IRB, University of Miami IRB, and University of Missouri–Kansas City IRB.

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Author Contributions

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 article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

PJW is or was an employee of Alkermes, Inc., and may own stock in the company; has served as a consultant for Alkermes, Anavex, Boehringer Ingelheim, Bristol Myers Squibb, Delpor, Lyndra, and MapLight; has served as a promotional speaker for Alkermes, Bristol Myers Squibb, and Neurocrine; and has served on an advisory board for Alkermes, Delpor, Küleon, and Teva.

LNS, MJD, CA, and JAM are or were employees of Alkermes, Inc., at the time this research was conducted and may own stock in the company.

EDA has consulted or served on advisory boards for Alkermes, Boehringer Ingelheim, Clinical Care Options, CME Outfitters, CMEology, Healthcare Global Village, Lundbeck/Otsuka, and VML Health and has received research funding from Alkermes, Boehringer Ingelheim, Janssen, Karuna, Neurocrine Biosciences, and Teva.

PDH has received fees for consulting and travel from Alkermes, BioXcel, Boehringer Ingelheim, Karuna, Minerva, and Sunovion; royalties for Brief Assessment of Cognition in Schizophrenia (owned by VeraSci, Inc.); and grant support from Stanley Medical Research Foundation and Takeda; and is chief scientific officer with i-Function, Inc.

JMK has been a consultant for or received honoraria from Alkermes, Allergan, Boehringer Ingelheim, Cerevel, Click Therapeutics, Dainippon Sumitomo, HLS, Indivior, Intra-Cellular Therapies, Janssen, J&J, Karuna, LB Pharmaceuticals, Lundbeck, Merck, Minerva, Neumora, Neurocrine Biosciences, Newron, Novartis, Otsuka, Reviva, Roche, Saladax Biomedical, Sunovion, Takeda, and Teva; has received grant support from Otsuka, Lundbeck, Janssen, and Sunovion; and is a shareholder of LB Pharmaceuticals and the Vanguard Research Group.

SRS is an employee of The University of Texas at Austin College of Pharmacy; was appointed to the Texas Health and Human Services Commission, San Antonio State Hospital, and the UT Health San Antonio Long School of Medicine; has served as consultant for Alkermes, Genomind, Janssen, Karuna, and Otsuka; has participated on the speakers' bureau for Neurocrine, Otsuka PsychU, Teva, Texas Society of Health-System Pharmacists, and, on occasion, for several professional organizations; serves on the Business Development Council for the American Association of Psychiatric Pharmacists; has served as expert witness on both defendant and plaintiff sides; and has no direct stock ownership in any pharmaceutical corporation.

JT was an employee of Worldwide Clinical Trials at the time this research was conducted.

DIV has served as consultant for and received research grant funding from Alkermes; served as a consultant, speaker, and advisory board participant for Otsuka; served as a consultant and speaker for Janssen; and served as an advisory board participant for Lyndra. The authors report no other conflicts of interest in this work.

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