Inpatient Initiation of the Long-Acting Injectable Antipsychotic Aripiprazole Lauroxil for the Treatment of Acute Exacerbations of Schizophrenia

Peter J. Weiden, MD,[1] Jelena Kunovac, MD, MS,[2-4] Shifang Liu, PhD,[5] Daniel J. Kim, PhD,[5] James A. McGrory, PhD[5]

[1]Renaissance School of Medicine at Stony Brook University, Stony Brook, NY, USA; [2]Redbird Research, Las Vegas, NV, USA; [3]Excell Research, Oceanside, CA, USA; [4]University of Nevada, Las Vegas, NV, USA; [5]Alkermes, Inc., Waltham, MA, USA

BACKGROUND

- Long-acting injectable (LAI) antipsychotic formulations are used for maintenance treatment of patients with schizophrenia but are considered less frequently for managing acute symptom exacerbations[1]
- Early LAI antipsychotic formulations were limited, requiring a prolonged period of daily oral antipsychotic supplementation to quickly achieve therapeutic plasma concentrations after initiation[2,3]
- Advances in formulation technology now allow rapid attainment of target plasma levels within days, reducing or eliminating the need for oral supplementation at initiation[2]
  - The LAI antipsychotic aripiprazole lauroxil (AL) has a 1-day initiation option that allows full onboarding of the LAI within a short hospital stay[4]
- Despite these advances, many clinicians rely solely on oral antipsychotic therapy in the inpatient setting[5,6]
- The ALPINE study (ClinicalTrials.gov identifier NCT03345979) was a 25-week, phase 3b, double-blind, randomized trial assessing the efficacy and safety of AL every-2-months initiated with the 1-day regimen during a 2-week inpatient period and in the 23 weeks after discharge[7]
  - AL treatment was associated with statistically significant reductions in Positive and Negative Syndrome Scale (PANSS) Total score at the 4- and 25-week endpoints
  - The study included an active LAI control with known efficacy for treating symptoms of schizophrenia (paliperidone palmitate [PP])

OBJECTIVE

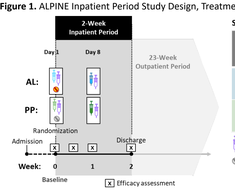
- The objective of this post hoc analysis was to evaluate the initial response to AL, initiated using the 1-day regimen, during a 2-week inpatient hospitalization for the treatment of acute schizophrenia

METHODS

Study Design

- Details of the ALPINE study design have been published previously[7]
  - This post hoc analysis focuses on the 2-week inpatient period; the outpatient period is assessed in a companion poster (Poster #23)
- Patients randomly assigned to AL received the 1-day initiation regimen on day 1, followed by their first dose of AL 1064 mg every-2-months on day 8 (**Figure 1**)
  - Initiation regimen: 1 injection of AL NanoCrystal Dispersion formulation (AL_{NCD}) and a single 30-mg oral dose of aripiprazole
  - No oral supplementation was given after day 1
- The active control was paliperidone palmitate (PP)

Figure 1. ALPINE Inpatient Period Study Design, Treatment, and Patient Population



Study Treatments

LAI	Day 1 (Initiation)	Day 8[a]	
		Dosage	Coverage Duration
AL	AL_{NCD} 1 30-mg dose OA	AL 1064 mg	2 months
PP	PP 234 mg	PP 156 mg	1 month

Placebo injection[b]
Placebo pill[c]

Study Population:
- Adults meeting *DSM-5* criteria for schizophrenia
- Hospitalized for acute symptoms (onset ≤2 months)
- PANSS Total score of 80–120

[a]The first AL injection can be administered on the same day as AL_{NCD} or ≤10 days afterward. The first PP 156-mg injection must be administered 8 days after the PP 234-mg injection; therefore, AL was administered on day 8 in ALPINE. [b]Because AL and PP use different injection sites, day 1 and day 8 injections were given with a placebo injection in the opposite site to maintain blinding. [c]Because the 1-day AL initiation regimen includes a 30-mg oral dose of aripiprazole, patients assigned to PP were administered an oral placebo tablet.
AL, aripiprazole lauroxil; AL_{NCD}, AL NanoCrystal Dispersion formulation; *DSM-5*, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; LAI, long-acting injectable; OA, oral aripiprazole; PANSS, Positive and Negative Syndrome Scale; PP, paliperidone palmitate.

Assessments

- Efficacy was assessed based on the PANSS Total score and PANSS Marder Factors[8]; early response was defined as ≥20% reduction in PANSS Total score from baseline to discharge
- Safety was assessed based on adverse events (AEs)

Post Hoc Analysis

- Data from the baseline (day 1, predose) and day 4, 8, and 15 assessments were included in the post hoc analysis
- Efficacy outcomes were analyzed using a mixed model for repeated measures approach

Patients

Table 1. Demographics and Baseline Clinical Characteristics[a]

Characteristics	Aripiprazole Lauroxil (n=99)	Paliperidone Palmitate (n=101)
Age, mean (SD), years	43.5 (9.7)	43.4 (10.8)
Sex, male, n (%)	73 (73.7)	76 (75.2)
Race,[b] n (%)		
Black or African American	72 (72.7)	78 (77.2)
White	25 (25.3)	17 (16.8)
Asian	2 (2.0)	4 (4.0)
BMI, mean (SD), kg/m²	28.2 (5.5)	27.9 (5.1)

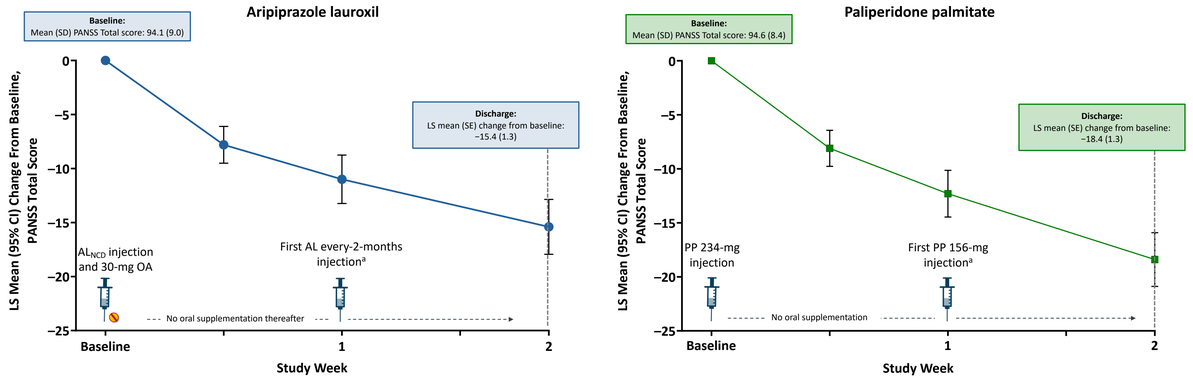
[a]Safety population (patients who received ≥1 dose of study drug). [b]Two patients in the paliperidone palmitate group reported >1 race and were reported as "multiple races."
BMI, body mass index.

RESULTS

AL treatment of acute schizophrenia was initiated using a 1-day regimen during a 2-week inpatient period

2-Week Efficacy

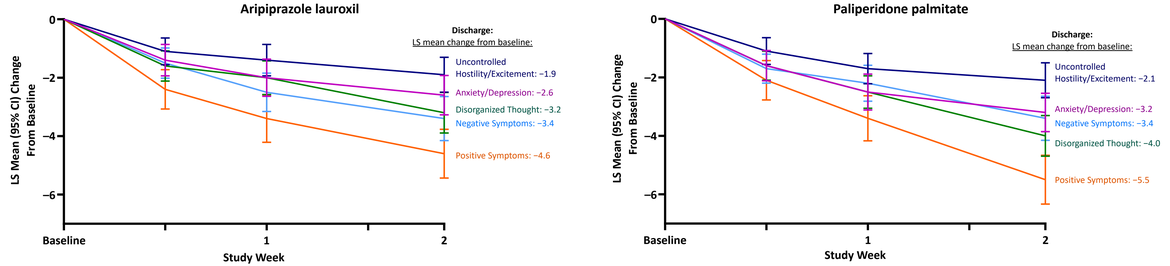
Figure 2. LS Mean Changes From Baseline in PANSS Total Score During the 2-Week Inpatient Period



[a]The first AL injection can be administered on the same day as AL_{NCD}, or up to 10 days afterward. The first PP 156-mg injection must be administered 8 days after the PP 234-mg injection; therefore, AL was administered on day 8 in ALPINE.
AL, aripiprazole lauroxil; AL_{NCD}, aripiprazole lauroxil NanoCrystal Dispersion formulation; LS, least squares; OA, oral aripiprazole; PANSS, Positive and Negative Syndrome Scale; PP, paliperidone palmitate.

- **No statistically significant differences in PANSS Total scores were observed between AL and PP at any assessment**
- **By discharge, 55.2% (53/96) of AL-treated patients had met the early treatment response criterion of ≥20% improvement from baseline in PANSS Total score during the inpatient period (PP, 60.6% [60/99])**

Figure 3. LS Mean Changes From Baseline in Marder Factor[a] Scores During the 2-Week Inpatient Period



[a]Marder factors include positive symptom items: delusions (P1), hallucinatory behavior (P3), grandiosity (P5), suspiciousness (P6), stereotyped thinking (N7), somatic concern (G1), unusual thought content (G9), and lack of judgment and insight (G12); negative symptom items: blunted affect (N1), emotional withdrawal (N2), poor rapport (N3), passive/apathetic social withdrawal (N4), lack of spontaneity (N6), motor retardation (G7), and active social avoidance (G16); disorganized thought items: conceptual disorganization (P2), difficulty in abstract thinking (N5), mannerisms and posturing (G5), poor attention (G11), disturbance of volition (G13), preoccupation (G15), and disorientation (G10); uncontrolled hostility/excitement items: excitement (P4), hostility (P7), uncooperativeness (G8), and poor impulse control (G14); and anxiety/depression items: anxiety (G2), guilt (G3), tension (G4), and depression (G6).[8]
LS, least squares.

2-Week Safety

- Most AEs reported in the first 2 weeks of treatment were mild (AL, 43.4%; PP, 29.7%) or moderate (AL, 8.1%; PP, 22.8%) in severity
- Serious AEs were reported for 2 AL-treated patients (generalized tonic-clonic seizure, worsening schizophrenia) and 0 PP-treated patients

Table 2. AEs Reported During the 2-Week Inpatient Period

Patients, n (%)	Aripiprazole Lauroxil (n=99)	Paliperidone Palmitate (n=101)
Patients with any AE	**53 (53.5)**	**53 (52.5)**
AEs reported by ≥3% of patients in either treatment group		
Injection site pain	15 (15.2)	25 (24.8)
Akathisia	9 (9.1)	10 (9.9)
Headache	5 (5.1)	6 (5.9)
Somnolence	4 (4.0)	7 (6.9)
Dystonia[a]	4 (4.0)	6 (5.9)
Constipation	3 (3.0)	3 (3.0)
Dizziness	3 (3.0)	3 (3.0)
Agitation	3 (3.0)	1 (1.0)
Myalgia	3 (3.0)	1 (1.0)
Injection site induration	3 (3.0)	0
Increased appetite	2 (2.0)	3 (3.0)
Weight increased	1 (1.0)	6 (5.9)
Arthralgia	1 (1.0)	3 (3.0)
AEs leading to study discontinuation[b]	4 (4.0)[c]	6 (5.9)

[a]Includes Medical Dictionary for Regulatory Activities version 21.1 preferred terms of dystonia and oromandibular dystonia. [b]AEs leading to study discontinuation included injection site pain (n=2) and generalized tonic-clonic seizure and worsening schizophrenia (n=1 each) for aripiprazole lauroxil and injection site pain, abdominal pain upper, akathisia, blood prolactin increased, dizziness, galactorrhea, and oromandibular dystonia (n=1 each) for paliperidone palmitate. [c]One patient assigned to aripiprazole lauroxil discontinued due to injection site pain associated with a placebo injection.
AE, adverse event.

LIMITATIONS

- This post hoc analysis was limited to the inpatient period to specifically address early response; however, efficacy and safety results for the 23-week outpatient period of ALPINE are reported in a companion poster (Poster #23)
- The study was not designed for between-group comparisons; the primary study objective was to assess the AL formulations, which were investigational at the time of the study, using PP as an active control
- These inpatient findings were specific to AL and PP and may not generalize to treatment with other LAI antipsychotics

CONCLUSIONS

- To our knowledge, this is the first clinical study to evaluate the safety and efficacy of using the 2 LAIs that could be initiated without required prolonged oral coverage and therefore were suited for inpatient initiation in patients entering the hospital already exposed to the respective oral formulation
- Early response to AL or PP over 2 weeks was robust based on improvement in PANSS Total score and on symptom domains of clinical interest
- Safety and tolerability following 1-day initiation were consistent with the known profile of oral aripiprazole (with the addition of injection site pain) and with that of AL initiated using 3 weeks of oral aripiprazole supplementation
  - The 2-week safety of PP was also consistent with its known profile
- These post hoc analysis findings support the existing evidence for inpatient initiation of LAI treatment for acute exacerbations of schizophrenia that require hospitalization

REFERENCES

1. Citrome L. *CNS Spectr*. 2021;26:118-29. DOI: 10.1017/S1092852919000876. **2.** Jain R, et al. *CNS Spectr*. 2020;25(3):323-30. DOI: 10.1017/S1092852919000816. **3.** Krishna A, et al. *J Am Board Fam Med*. 2024;37(4):773-83. DOI: 10.3122/jabfm.2022.220425R2. **4.** Sommi RW, et al. *J Clin Psychiatry*. 2024;85:23m15132. DOI: 10.4088/JCP.23m15132. **5.** Velligan D, et al. *BMC Psychiatry*. 2025;25(1):232. DOI: 10.1186/s12888-025-06565-1. **6.** Olayinka O, et al. *Psychiatry J*. 2019;2019:8629030. DOI: 10.1155/2019/8629030. **7.** Weiden PJ, et al. *J Clin Psychiatry*. 2020;81:19m13207. DOI: 10.4088/JCP.19m13207. **8.** Marder SR, et al. *J Clin Psychiatry*. 1997;58(12):538-46. DOI: 10.4088/jcp.v58n1205.

Acknowledgments, disclosure information, and copies of this poster can be obtained through this QR (Quick Response) code. These materials are for personal use only and may not be reproduced without permission of Alkermes. For permission, contact USMedInfo@Alkermes.com.

Supported by funding from Alkermes, Inc.

Inpatient Initiation of the Long-Acting Injectable Antipsychotic Aripiprazole Lauroxil for the Treatment of Acute Exacerbations of Schizophrenia

Peter J. Weiden, MD,[1] Jelena Kunovac, MD, MS,[2-4] Shifang Liu, PhD,[5] Daniel J. Kim, PhD,[5] James A. McGrory, PhD[5]

[1]Renaissance School of Medicine at Stony Brook University, Stony Brook, NY, USA; [2]Redbird Research, Las Vegas, NV, USA; [3]Excell Research, Oceanside, CA, USA; [4]University of Nevada, Las Vegas, NV, USA; [5]Alkermes, Inc., Waltham, MA, USA

ACKNOWLEDGMENTS

This study was funded by Alkermes, Inc., Waltham, MA, USA. Medical writing and editorial support were provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Alkermes, Inc.

DISCLOSURES

PJW is a former employee of Alkermes, Inc., and has been a consultant for Alkermes, Lyndra, MapLight, and Teva.
JK is the founder of Altea Research Institute and a cofounder of Excell Research and is a consultant and/or serves on advisory boards for AstraZeneca, Bristol Myers Squibb, Janssen, Novartis, Otsuka, Pfizer, and Sunovion.
SL, DJK, and **JAM** are or were employees of Alkermes, Inc., and may own stock/options in the company.

Supported by funding from Alkermes, Inc.