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Supplementary Material

Article Title: Initiating Aripiprazole Lauroxil: Post Hoc Analysis of Safety and Tolerability of 1-Day and 21-Day Regimens

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

DISCLAIMER

Supplementary Table 1. 1-Day Regimen Study[1] and 21-Day Regimen Study[2]

Characteristics

	1-Day Regimen Study	**21-Day Regimen Study**
Design	Randomized, double blind, active controlled	Randomized, double blind, placebo controlled
Total study duration	25 weeks	12 weeks
Duration of inpatient stay after randomization	2 weeks, with ≤1 additional week if clinically necessary	2 weeks, or longer if clinically necessary (no maximum specified)
AL treatment arm(s)	AL 1064 mg (n=99)	AL 441 mg (n=207) AL 882 mg (n=208)
Comparator/control	Paliperidone palmitate	Placebo
AL initiation regimen		
Active medication	Day 1: AL_{NCD} IM (gluteal) plus single 30-mg dose of oral aripiprazole	Days 1−21: 15 mg/day of oral aripiprazole
Placebo to maintain blind[a]	Day 1: placebo injection (deltoid) plus single placebo tablet	None
First AL dose		
Active medication	Day 8: AL 1064 mg IM (gluteal)	Day 1: AL 441 or 882 mg IM (gluteal)
Placebo to maintain blind[a]	Day 8: placebo injection (deltoid)	None
Safety endpoint	Incidence of adverse events	Incidence of adverse events
Primary efficacy endpoint	Change from baseline in PANSS total score at week 4	Change from baseline in PANSS total score at week 12

[a]An IM placebo injection (deltoid) was administered on days 1 and 8 to match the timing and injection site of active comparator injections to maintain blinding.

AL=aripiprazole lauroxil; AL_{NCD}=aripiprazole lauroxil NanoCrystal Dispersion; IM=intramuscular; PANSS=Positive and Negative Syndrome Scale.

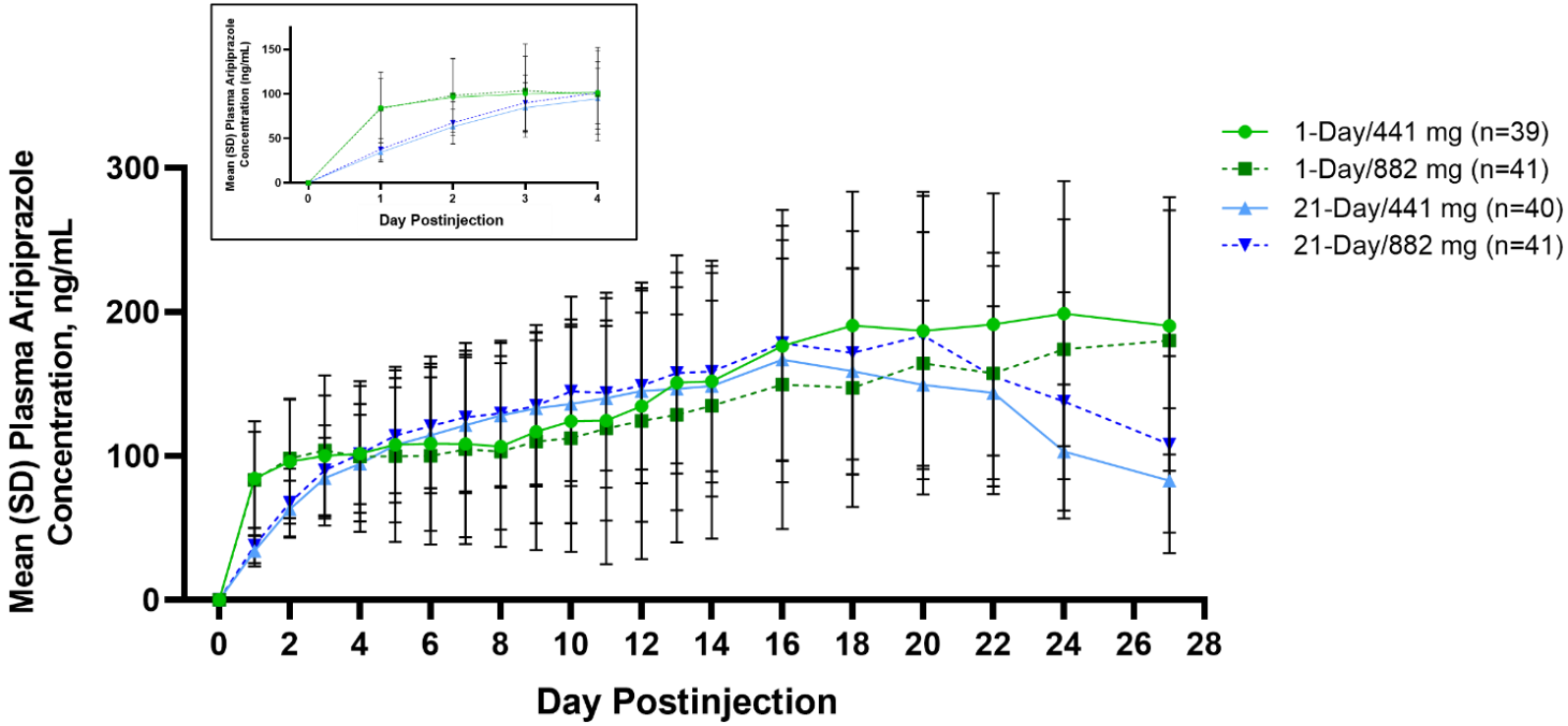
Supplementary Table 2. ISRs[a] and Akathisia: First 4 Study Weeks

	1-Day Regimen (n=99)	21-Day Regimen (n=415)
ISRs		
Day 1 injection, %		
Injection site pain	10.1	3.4
Injection site erythema	1.0	0
Injection site induration	1.0	0.2
Muscle swelling	1.0	0
Myalgia	1.0	0
Other hematoma	0	0.2
Other redness		0.2
Day 8 injection (1-day regimen only), %		
Injection site pain	9.2	–
Injection site induration	2.3	–
Injection site swelling	1.2	–
Akathisia		
Patients with akathisia, %		
Akathisia	9.1	10.8
Restlessness	1.0	2.4
Proportion of patients who received treatment for akathisia, n/N	8/9	4/45

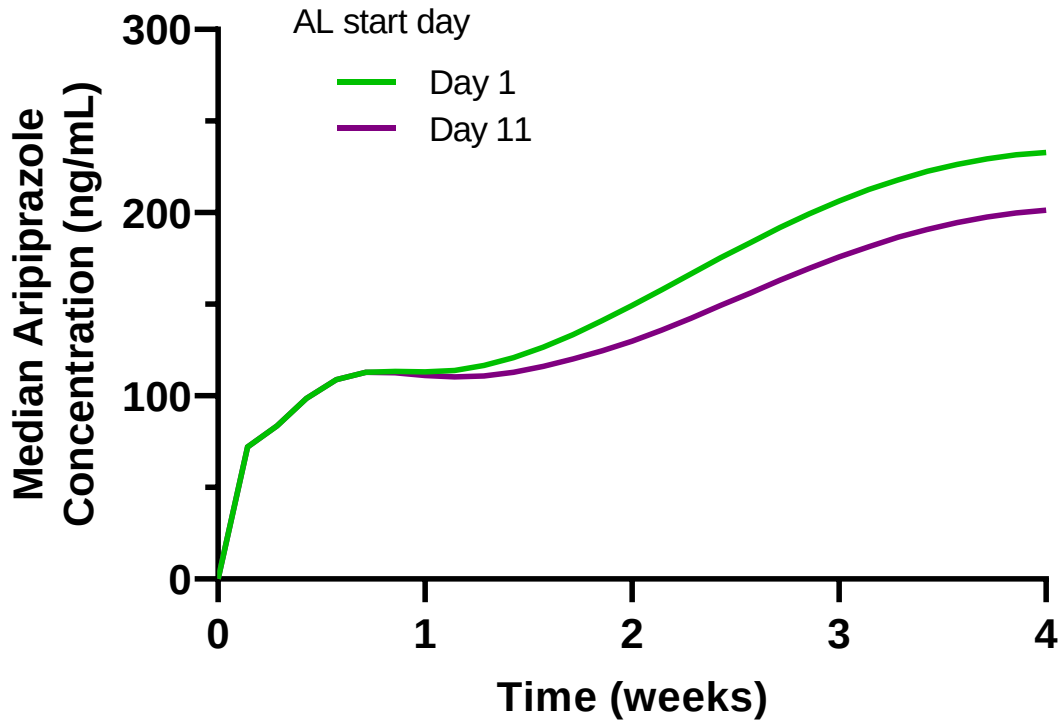
[a]Includes ISRs associated with first LAI AL injection with the 21-day regimen or with AL_{NCD} (day 1) and first LAI AL (day 8) injection with the 1-day injection.
AE=adverse event; AL_{NCD}=aripiprazole lauroxil NanoCrystal Dispersion; ISR=injection site reaction; LAI=long-acting injectable; n/N = number of patients receiving treatment for akathisia/number of patients with AEs of akathisia.

Supplementary Figure 1. Plasma Aripiprazole Concentrations After Initiation

A. Observed Plasma Aripiprazole Concentrations Over 28 Days After Initiation With the 1-Day and 21-Day Regimens (Inset: First 4 Days)



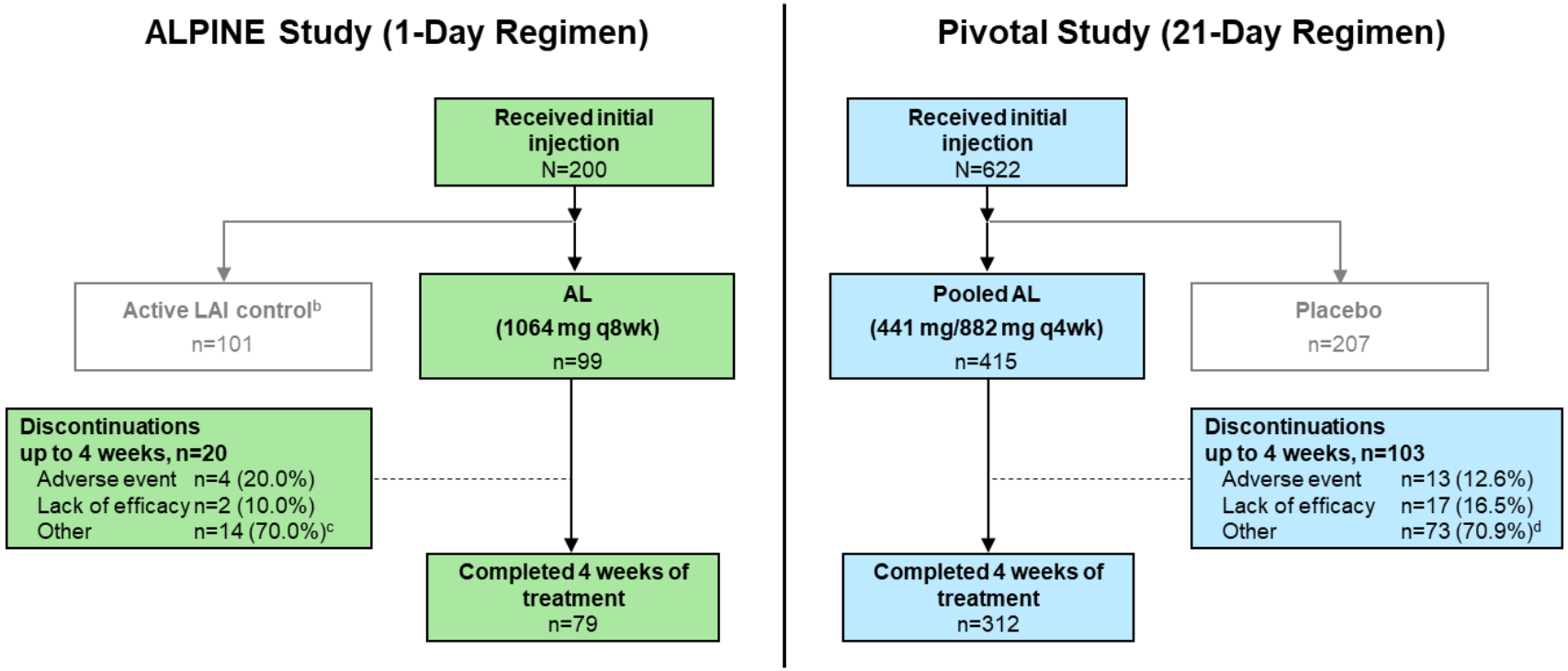
B. Median Simulated Aripiprazole Concentrations After Initiation of AL Using AL_{NCD} Plus 30 mg of Oral Aripiprazole, Modeled With Administration of AL on the Same Day as (Day 1) or up to 10 Days After (Day 11) the 1-Day Regimen[a]



[a]Panel A redrawn with permission from reference 3; panel B data used with permission from reference 4.

AL=aripiprazole lauroxil; AL_{NCD}=aripiprazole lauroxil NanoCrystal Dispersion.

Supplementary Figure 2. Patient Disposition, Post Hoc Analysis Population[a]



[a]Treatment groups shown in gray were not included in this post hoc analysis.

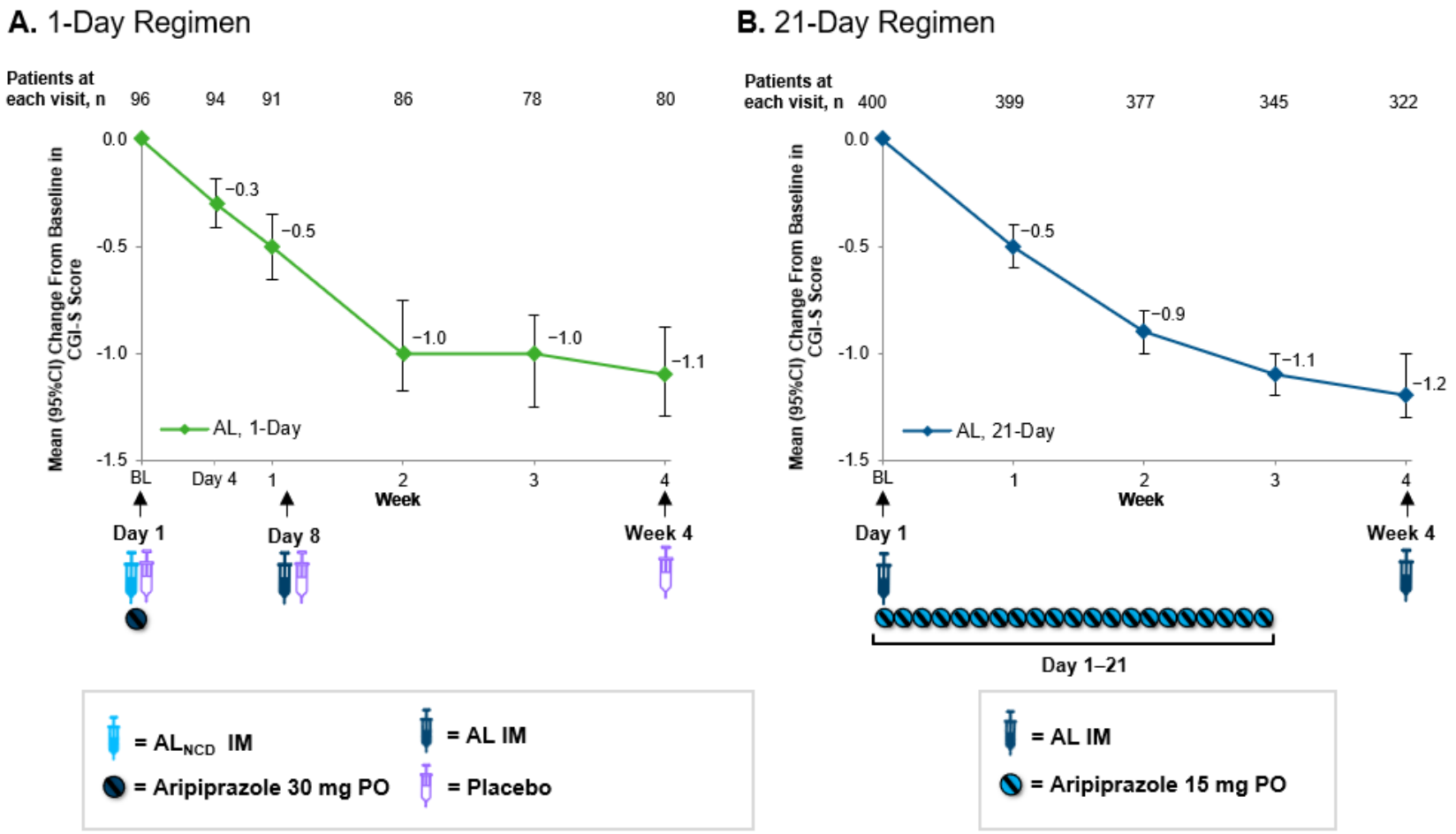
[b]Paliperidone palmitate served as an active control for the 1-day regimen study.

[c]Includes withdrawal by patient (n=10), loss to follow-up (n=3), and protocol deviation (n=1).

[d]Includes withdrawal by patient (n=48), loss to follow-up (n=14), protocol deviation (n=7), physician decision (n=3), and other reason (n=1).

AL=aripiprazole lauroxil; LAI=long-acting injectable; q4wk=every 4 weeks; q8wk=every 8 weeks.

Supplementary Figure 3. Mean Changes From Baseline in CGI-S Scores[a] During First 4 Weeks of Treatment (Observed Cases)



[a]Mean baseline CGI-S scores: 4.8 (1-day) and 4.9 (21-day).

AL_{NCD}=aripiprazole lauroxil NanoCrystal Dispersion; BL=baseline; CGI-S=Clinical Global Impression–Severity; CI=confidence interval; IM=intramuscular.

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