CNS Drugs

Supplementary Material

Title: Impact of long-acting injectable vs. oral antipsychotic treatment on all-cause discontinuation risk in people with early-phase schizophrenia and comorbid substance use disorder: A secondary analysis of the EULAST randomized trial

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SUD and no SUD definition

A seven-item scale according to the Mini-International Neuropsychiatric Interview 5 Plus (MINI) was used to stratify subjects into two distinct groups: “substance users” and “not substance users”. A subject was classified as a "substance user" if they responded "yes" to any of the following items: substance dependence lifetime (non-alcohol); substance dependence current (non-alcohol); substance abuse (non-alcohol) current; alcohol dependence current; alcohol abuse current; alcohol dependence lifetime; alcohol dependence lifetime. If a subject had missing responses to one or more of the aforementioned items but had provided a “yes" response to any of the remaining items, they were subsequently classified as a substance user. Among the substance users, a subject was considered to have “current substance use” (in contrast to only lifetime substance use), if they responded “yes” to any of the following items: substance dependence current (non-alcohol); substance abuse (non-alcohol) current; alcohol dependence current; alcohol abuse current.

The "not substance user" category was comprised of subjects who provided a "no" response to all the aforementioned items. In instances where a subject had responded "no" to some items and had no responses to the remaining items, also meaning a lack of "yes" response to any of the items, their substance use status was classified as unknown and they were excluded from the pool of subjects.

Supplementary Table 1. Demographics and clinical characteristics of the patients in "without SUD" sample.

Variable		Oral Antipsychotics Medication (N=154)	LAI Antipsychotics Medication (N=174)	P-value	Total (N=328)
Age, Mean (SD)		31.45 (10.33)	31.40 (9.45)	0.698[a]	31.42 (9.86)
Duration of Illness (Month), Mean (SD)		36.80 (24.33, n=154)	54.03 (148.55, n=174)	0.289[b]	45.94 (109.66)
Gender, N (%)	**Female**	55 (35.7%)	78 (44.8%)	0.093[b]	133 (40.5%)
	Male	99 (64.3%)	96 (55.2%)		195 (59.5%)
Treatment, N (%) (Medications)	**Aripiprazole**	77 (50.0%)	81 (46.6%)	0.533[b]	158 (48.2%)
	Paliperidone	77 (50.0%)	93 (53.4%)		170 (51.8%)
Race, N (%)	**Asian**	6 (3.9%)	1 (0.6%)	0.159[b]	7 (2.1%)
	Black	6 (3.9%)	11 (6.9%)		17 (5.2%)
	White	130 (84.4%)	149 (85.6%)		279 (85.1%)
	Other	12 (7.8%)	13 (7.5%)		25 (7.6%)
Years of Education, Mean (SD)		11.7 (3.05)	12.29 (2.76)	0.022[b]	12.01 (2.91)
Living Independently, N (%)		31 (20.5%)	28 (16.3%)	0.387[b]	59 (18.3%)
Major Depressive Disorder (Current), N (%)		5 (3.2%)	1 (0.6%)	0.072[b]	6 (1.8%)
Suicidality (current), N (%)		29 (18.8%)	25 (14.4%)	0.448[b]	54 (16.5%)
PANSS Positive, Mean (SD)		17.54 (5.88)	17.22 (5.95)	0.730[a]	17.37 (5.91)
PANSS Negative, Mean (SD)		20.94 (6.13)	20.48 (6.54)	0.508[a]	20.69 (6.34)
PANSS General, Mean (SD)		38.13 (9.54)	37.19 (9.38)	0.292[a]	37.63 (9.45)
PANSS Total, Mean (SD)		76.61 (18.43)	74.88 (17.95)	0.378[a]	75.69 (18.17)
CGI Severity), Mean (SD)		4.34 (0.896, n=150)	4.41 (1.075, n=172)	0.257[a]	4.38 (0.995, 322)
Overall functioning (PSP), Mean (SD)		51.52 (16.78, n=150)	53.24 (16.56, n=170)	0.310[a]	52.43 (16.67, n=320)

Abbreviations: PANSS – Positive and Negative Syndrome Scale for Schizophrenia; CGI – Clinical Global Impression; PSP – Personal and Social Performance scale; SD – Standard Deviation of the mean.

Supplementary Table 2. Demographics and clinical characteristics of all patients. a: Mann-Whitney U test (Z Score), b: Pearson Chi-square test.

Variable		Oral Antipsychotics Medication (N=223)	LAI Antipsychotics Medication (N=248)	P-value	Total (N=471)
Age, Mean (SD)		30.84 (10.03)	30.47 (9.42)	0.9[a]	30.64 (9.703)
Duration of Illness (Month), Mean (SD)		41.92 (94.83, n=223)	48.75 (125.20, n=248)	0.2[a]	45.52 (111.79)
Gender, N (%)	**Female**	68 (30.5%)	89 (35.9%)	0.2[b]	157 (33.0%)
	Male	155 (69.5%)	159 (64.1%)		314 (67.0%)
Treatment, N (%) (Medications)	**Aripiprazole**	111 (49.8%)	120 (48.4%)	0.7[b]	231 (49.0%)
	Paliperidone	112 (50.2%)	128 (51.6%)		240 (51.0%)
Race, N (%)	**Asian**	10 (4.5%)	6 (2.4%)	0.4[b]	16 (3.4%)
	Black	14 (6.3%)	20 (8.1%)		34 (7.2%)
	White	178 (79.8%)	204 (82.2%)		382 (81.1%)
	Other	21 (9.4%)	18 (7.3%)		39 (8.3%)
Years of Education, Mean (SD)		11.65 (2.94)	12.09 (2.67)	0.05[a]	11.88 (2.81)
Living Independently, N (%)		56 (25.1%)	50 (20.2%)	0.18[b]	106 (22.5%)
Major Depressive Disorder (Current), N (%)		6 (2.7%)	5 (2.0%)	0.62[b]	11 (2.3%, n=471)
Suicidality (current), N (%)		53 (23.8%)	57 (23.0%)	0.48[b]	110 (23.4%, n=471)
Alcohol Abuse, N (%)		35 (16.1%)	42 (17.3%)	0.80[b]	77 (16.7%)
Substance Abuse, N (%)		57 (25.7%)	60 (24.2%)	0.74[b]	117 (24.9%)
PANSS Positive, Mean (SD)		17.62 (6.12)	17.21 (5.91)	0.65[a]	17.40 (6.01)
PANSS Negative, Mean (SD)		20.14 (6.59)	19.83 (6.53)	0.65[a]	19.97 (6.55)
PANSS General, Mean (SD)		37.51 (9.93)	37.07 (9.56)	0.65[a]	37.28 (9.73)
PANSS Total, Mean (SD)		75.27 (19.21)	74.11 (18.08)	0.56[a]	74.65 (18.60)
CGI Severity, Mean (SD)		4.33 (0.96, n=213)	4.40 (1.03, n=244)	0.23[a]	4.37 (0.996, n=457)
Overall functioning (PSP), Mean (SD)		50.99 (17.06, n=211)	52.91 (15.64, n=241)	0.26[a]	52.01 (16.33, n=452)

Abbreviations: PANSS – Positive and Negative Syndrome Scale for Schizophrenia; CGI – Clinical Global Impression; PSP – Personal and Social Performance scale; SD – Standard Deviation of the mean.

STROBE statement: Reporting guidelines checklist for cohort, case-control and cross-sectional studies

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
TITLE AND ABSTRACT			
	1a	Indicate the study's design with a commonly used term in the title or the abstract	1-2
	1b	Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
INTRODUCTION			
Background and objectives	2	Explain the scientific background and rationale for the investigation being reported	4-5
	3	State specific objectives, including any pre-specified hypotheses	5
METHODS			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6a	Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	5-7
	6b	Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case Variables	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/measurements	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.	7-8

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
Bias	9	Describe any efforts to address potential sources of bias.	5-8
Study size	10	Explain how the study size was arrived at	5-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why .	7-8
Statistical methods	12a	Describe all statistical methods, including those used to control for confounding	7-8
	12b	Describe any methods used to examine subgroups and interactions	7-8
	12c	Explain how missing data were addressed	7-8
	12d	Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	7-8
	12e	Describe any sensitivity analyses	
RESULTS			
Participants	13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
	13b	Give reasons for non-participation at each stage	Figure 1 5-7
	13c	Consider use of a flow diagram	Figure 1
Descriptive Data	14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
	14b	Indicate number of participants with missing data for each variable of interest	8-9 Figure 1
	14c	Cohort study—Summarise follow-up time (eg, average and total amount)	5-7
Outcome Data	15*	Cohort study—Report numbers of outcome events or summary measures over time Case-control study—Report numbers in each exposure category, or summary measures of exposure Cross-sectional study—Report numbers of outcome events or summary measures	5-7 9-11

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
Main Results	16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
	16b	Report category boundaries when continuous variables were categorized	9-11
	16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11
	16d	Report results of any adjustments for multiple comparisons	
Other Analyses	17a	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	10
	17b	If numerous genetic exposures (genetic variants) were examined, summarize results from all analyses undertaken	
	17c	If detailed results are available elsewhere, state how they can be accessed	
DISCUSSION			
Key Results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results Other information	12-13
FUNDING			
	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.