FLUOXETINE VERSUS PLACEBO TREATMENT OF DEPRESSION AND CO-MORBID SUBSTANCE USE

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OBJECTIVE

The primary objective of this study is to examine the efficacy and tolerability of fluoxetine treatment of depressed adolescents with a co-morbid substance-related disorder.

METHODS

Outpatients aged 12-17 years meeting DSM-IV diagnostic criteria for a major depressive disorder or dysthymic disorder with a co-morbid substance-related disorder were eligible to enroll.

Patients also had to suffer from depressive symptoms of at least moderate severity (CDRS-R ≥ 40).

Eligible subjects were randomized to receive either fluoxetine or placebo in a double-blind fashion.

DOSING

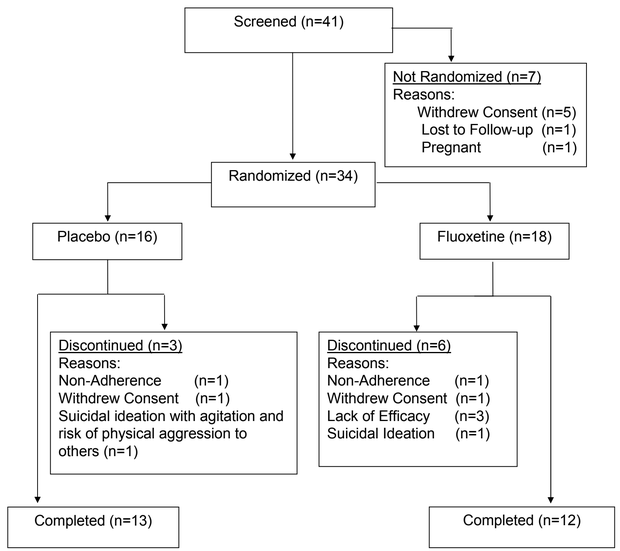
Subjects received either 10mg fluoxetine or matching placebo for the first 4 weeks of treatment.

At week 4, the subject's dose could be increased to 20mg fluoxetine or matching placebo.

Demographics

	Fluoxetine (n=18)	Placebo (n=16)	Total (n=34)
Ethnicity, n (%)			
White	14 (78)	11 (19)	25 (74)
African American	3 (17)	3 (69)	6 (18)
Other	1 (5)	2 (12)	3 (9)
Gender (%)			
Males	14 (78)	15 (94)	29 (85)
Females	4 (22)	1 (6)	5 (15)
Current Depressive Disorder (%)			
MDD	15 (83)	13 (81)	28 (82)
Other	3 (17)	3 (19)	6 (18)
Substance Use Disorders (%)			
Alcohol	2 (11)	3 (19)	5 (15)
Cannabis	10 (56)	9 (56)	19 (56)
Polysubstance	7 (39)	7 (44)	14 (41)
Age (s.d., years)	16.55 (1.11)	16.35 (1.08)	16.46 (1.08)

Patient Disposition

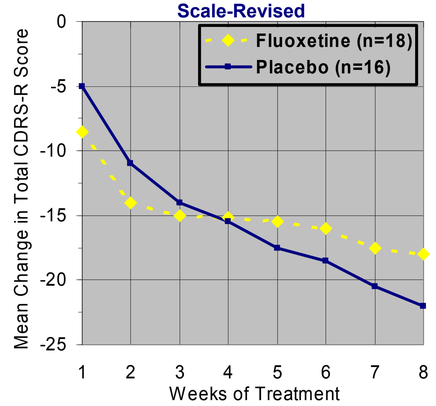


RESULTS

•Enrollment into the trial was stopped after the interim analysis was performed, after 34 patients had been enrolled, on the basis of the pre-specified futility stopping rule.

•Comparison of the primary outcome via mixture model analysis crossed the a priori futility boundary for early stopping with acceptance of the null hypothesis of no treatment difference in mean change in CDRS-R total score (estimated treatment difference =0.19,S.E.=0.58, F=0.14, p=.74).

Mean change from baseline for fluoxetine and placebo treated patients on the Children's Depression Rating Scale-Revised



In the random effects regression model, there was no significant treatment by visit interaction (p=.14), indicating no difference between treatment groups in mean change in CDRS-R score over time.

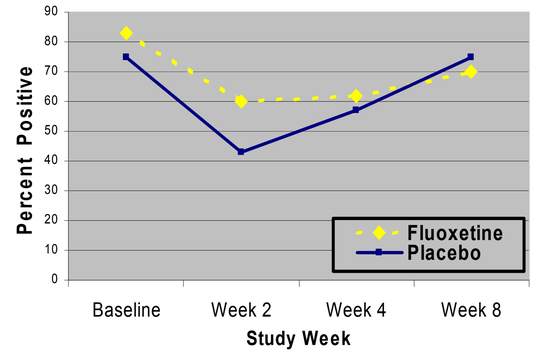
Change in Baseline to Endpoint in Depressive Symptomatology and Psychosocial Functioning

	Baseline	Endpoint	Change	p*	F
CDRS-R					
Fluoxetine	53.0(2.32)	34.60(3.22)	-18.40(2.94)	0.33	0.98
Placebo	53.94(2.46)	31.31(3.42)	-22.63(3.12)		
CGI-S					
Fluoxetine	4.28(0.15)	2.88(0.28)	-1.39(0.28)	0.71	0.07
Placebo	4.37(0.16)	2.87(0.30)	-1.50(0.30)		
CGI-I					
Fluoxetine	--	2.61(0.32)	--	0.79	0.14
Placebo	--	2.44(0.34)	--		
BDI					
Fluoxetine	17.20(3.10)	7.62(1.96)	-9.58(3.29)	0.34	0.95
Placebo	13.00(3.33)	8.12(2.11)	-4.88(3.54)		
BHS					
Fluoxetine	7.33(1.38)	4.07(1.10)	-3.27(1.38)	0.61	0.26
Placebo	7.69(1.49)	5.46(1.18)	-2.23(1.48)		
CGAS					
Fluoxetine	53.06(2.06)	69.63(3.62)	16.56(3.50)	0.72	0.13
Placebo	51.21(2.20)	65.93(3.87)	14.71(3.75)		

NOTE: Values represent mean (SE) from fixed effects parameter estimates. CDRS-R=Children's Depression Rating Scale-Revised; CGI-S=Clinical Global Impressions - Severity scale; CGI-I=Clinical Global Impressions - Improvement Scale; BDI=Beck Depression Inventory; BHS=Beck Hopelessness Scale; CGAS=Children's Global Assessment of Functioning

* Random effects regression analyses using baseline and endpoint values: p value for difference in mean change between treatment groups, using Type III difference of least square means.

Percent of patients with positive drug screens who received fluoxetine or placebo for 8 weeks



Rates of positive urine drug screens did not differ between treatment groups (p=0.65).

Most common adverse events by treatment group

Symptom		Total	Fluoxetine	Placebo	P
		34 (100%)	18 (53%)	16 (47%)	
Headache	Present (N, %)	18 (53%)	10 (56%)	8 (50%)	0.75
Nasal Congestion	Present (N, %)	13 (38%)	7 (39%)	6 (38%)	0.67
Drowsiness	Present (N, %)	8 (24%)	6 (33%)	2 (13%)	0.97
Nausea/Vomiting	Present (N, %)	8 (24%)	5 (28%)	3 (19%)	0.85
Stomach Pain	Present (N, %)	7 (21%)	2 (11%)	5 (31%)	0.21
Diarrhea	Present (N, %)	4 (12%)	2 (11%)	2 (13%)	0.65

CONCLUSIONS

Fluoxetine was not superior to placebo in alleviating depressive symptoms in adolescents with depression and a substance use disorder.

Those patients treated with fluoxetine, did not show a significantly greater decrease in their substance use in comparison to those patients who received placebo.

ACKNOWLEDGEMENTS

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