



THE JOURNAL OF CLINICAL PSYCHIATRY

THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL PSYCHOPHARMACOLOGY

Supplementary Material

Article Title: Increasing Versus Maintaining the Dose of Olanzapine or Risperidone in Schizophrenia Patients Who Did Not Respond to a Modest Dosage: A Double-Blind Randomized Controlled Trial

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DOI Number: 10.4088/JCP.15m10490

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Supplementary eTable 1. Baseline Demographic and Clinical Characteristics of Participants with Total Duration of Antipsychotic Treatment of <0.5 years

Characteristics	Increment (n=18)	Continuation (n=20)	Statistics	P-value
Age, years, mean (s.d.)	45.4 (12.4)	48.1 (18.0)	$t(36)=0.51$	0.61
Women, n (%)	12 (66.7%)	12 (60.0%)	$\chi^2(1)=0.18$	0.67
Race				
Asian, n (%)	18 (100.0%)	20 (100.0%)	$z=0.00$	1.00
Body weight, kg, mean (s.d.)	54.8 (10.7)	58.1 (13.3)	$t(36)=0.83$	0.42
Inpatient, n (%)	18 (100.0%)	19 (95.0%)	n.a.	1.00 ^a
Duration of illness, years, mean (s.d., median)	5.4 (8.8, 3.0)	6.4 (7.6, 3.3)	$z=-0.16$	0.87
Duration of current episode, years, mean (s.d., median)	3.7 (9.0, 0.7)	1.9 (2.2, 0.9)	$z=-0.73$	0.48
Total duration of antipsychotic treatment, years, mean (s.d.)	0.17 (0.09)	0.15 (0.09)	$z=-1.10$	0.29
Duration of current antipsychotic regimen, years, mean (s.d.)	0.10 (0.03)	0.08 (0.01)	$z=-1.45$	0.21
Medication			$\chi^2(1)=3.71$	0.054
Olanzapine, n (%)	11 (61.1%)	6 (30.0%)		
Risperidone, n (%)	7 (38.9%)	14 (70.0%)		
Concomitant medications				
Antidepressant, n (%)	4 (22.2%)	0 (0.0%)	n.a.	0.041^a
Mood stabilizer, n (%)	1 (5.6%)	1 (5.0%)	n.a.	1.00 ^a
PANSS total score, mean (s.d.)	85.3 (13.9)	88.3 (11.6)	$t(36)=0.69$	0.50
PANSS positive score, mean (s.d.)	20.6 (4.2)	22.1 (3.6)	$t(36)=1.15$	0.26
PANSS negative score, mean (s.d.)	22.6 (5.4)	22.1 (4.3)	$t(36)=-0.32$	0.75
PANSS general score, mean (s.d.)	42.1 (7.4)	44.1 (6.1)	$t(36)=0.86$	0.40
CGI-S score, mean (s.d.)	4.7 (0.8)	4.8 (0.8)	$z=-1.29$	0.78
GAF score, mean (s.d.)	38.4 (11.4)	37.4 (9.4)	$t(36)=-0.30$	0.76
SAS total score, mean (s.d.)	1.2 (1.5)	2.2 (1.6)	$z=-2.05$	0.048
BARS global clinical assessment score, mean (s.d.)	0.7 (0.7)	0.8 (0.5)	$z=-0.52$	0.65
AIMS total score (1-7 items), mean (s.d.)	0.8 (1.2)	1.2 (1.1)	$z=-1.26$	0.25

^a. Fisher's exact test.

P-values of <0.05 are shown in bold.

s.d., standard deviation; PANSS, Positive and Negative Syndrome Scale; CGI-S, Clinical Global Impression-Severity of Illness; GAF, Global Assessment of Functioning; SAS, Simpson-Angus Scale; BARS, Barnes Akathisia Rating Scale; AIMS, Abnormal Involuntary Movement Scale; n.a., not available

Supplementary eTable 2. Baseline Demographic and Clinical Characteristics of Participants with Baseline Plasma Olanzapine or Risperidone Concentrations of <20 ng/mL

Characteristics	Increment (n=13)	Continuation (n=16)	Statistics	P-value
Age, years, mean (s.d.)	44.6 (12.4)	44.9 (18.0)	$t(27)=0.05$	0.96
Women, n (%)	6 (46.2%)	9 (56.3%)	$\chi^2(1)=0.29$	0.59
Race				
Asian, n (%)	13 (100.0%)	16 (100.0%)	$z=0.00$	1.00
Body weight, kg, mean (s.d.)	66.7 (15.4)	57.8 (8.8)	$t(18)=-1.79$	0.09
Inpatient, n (%)	13 (100.0%)	16 (100.0%)	n.a.	1.00 ^a
Duration of illness, years, mean (s.d.)	15.6 (12.6)	15.6 (14.2)	$t(27)=-0.00$	1.00
Duration of current episode, years, mean (s.d.)	0.9 (2.1)	0.8 (1.2)	$z=-0.05$	0.96
Total duration of antipsychotic treatment, years, mean (s.d.)	11.7 (13.9)	13.3 (14.4)	$z=-0.18$	0.86
Duration of current antipsychotic regimen, years, mean (s.d.)	0.08 (0.01)	0.10 (0.03)	$z=-1.57$	0.12
Medication			n.a.	0.71 ^a
Olanzapine, n (%)	5 (38.5%)	5 (31.3%)		
Risperidone, n (%)	8 (61.5%)	11 (68.7%)		
Concomitant medications				
Antidepressant, n (%)	2 (15.4%)	2 (12.5%)	n.a.	1.00 ^a
Mood stabilizer, n (%)	4 (30.8%)	8 (50.0%)	$\chi^2(1)=1.09$	0.30
PANSS total score, mean (s.d.)	86.8 (16.7)	97.3 (15.9)	$t(27)=1.67$	0.11
PANSS positive score, mean (s.d.)	22.4 (5.3)	24.3 (3.3)	$t(27)=1.12$	0.27
PANSS negative score, mean (s.d.)	21.6 (4.0)	24.3 (5.1)	$t(27)=1.50$	0.14
PANSS general score, mean (s.d.)	42.8 (8.8)	48.8 (9.1)	$t(27)=1.71$	0.65
CGI-S score, mean (s.d.)	4.8 (0.9)	5.2 (0.7)	$z=-0.85$	0.39
GAF score, mean (s.d.)	38.7 (12.2)	33.4 (8.5)	$t(27)=-1.33$	0.20
SAS total score, mean (s.d.)	1.5 (1.3)	2.1 (1.3)	$z=-0.93$	0.35
BARS global clinical assessment score, mean (s.d.)	0.6 (0.6)	1.2 (0.9)	$z=-1.63$	0.10
AIMS total score (1-7 items), mean (s.d.)	1.2 (1.1)	1.3 (1.7)	$z=-0.37$	0.71

^a. Fisher's exact test.

P-values of <0.05 are shown in bold.

s.d., standard deviation; PANSS, Positive and Negative Syndrome Scale; CGI-S, Clinical Global Impression-Severity of Illness; GAF, Global Assessment of Functioning; SAS, Simpson-Angus Scale; BARS, Barnes Akathisia Rating Scale; AIMS, Abnormal Involuntary Movement Scale; n.a., not available

Supplementary eTable 3. Outcome Measures in Participants with Baseline Plasma Olanzapine or Risperidone Concentrations of <20 ng/mL

Characteristics	Increment	Continuation	Statistics	P-value
Completion rate, (%)	11/13 (84.6%)	12/16 (75.0%)	n.a.	0.66 ^a
PANSS total score change, mean (s.d.) (PP)	-11.8 (9.3)	-7.0 (6.5)	$t(21)=-1.39$	0.18
PANSS total score change, mean (s.d.) (ITT)	-10.0 (9.5)	-5.3 (6.4)	$t(27)=-1.55$	0.13
PANSS positive score change, mean (s.d.) (PP)	-4.3 (3.5)	-3.1 (2.5)	$t(21)=-0.90$	0.38
PANSS positive score change, mean (s.d.) (ITT)	-3.6 (3.6)	-2.3 (2.6)	$t(27)=-1.10$	0.28
PANSS negative score change, mean (s.d.) (PP)	-2.3 (3.3)	-1.3 (1.7)	$z=-0.38$	0.71
PANSS negative score change, mean (s.d.) (ITT)	-1.9 (3.1)	-1.0 (1.6)	$t(17)=-0.93$	0.37
PANSS general score change, mean (s.d.) (PP)	-5.3 (3.4)	-2.6 (4.8)	$t(21)=-1.47$	0.16
PANSS general score change, mean (s.d.) (ITT)	-4.5 (3.7)	-1.9 (4.3)	$t(27)=-1.62$	0.12
Response rate, (%) (PP)	27.3% (3/11)	0.0% (0/12)	n.a.	0.09 ^a
Response rate, (%) (ITT)	23.1% (3/13)	0.0% (0/16)	n.a.	0.08 ^a
CGI-GI, mean (s.d.)	2.7 (0.9)	3.1 (0.6)	$z=-0.97$	0.33
GAF score change, mean (s.d.) (PP)	9.8 (9.0)	5.8 (3.5)	$z=-1.24$	0.22
GAF score change, mean (s.d.) (ITT)	8.3 (9.0)	4.4 (3.9)	$z=-1.20$	0.23
SAS total score change, mean (s.d.) (PP)	0.4 (0.5)	0.7 (2.4)	$z=-0.74$	0.46
SAS total score change, mean (s.d.) (ITT)	0.3 (0.5)	0.5 (2.1)	$z=-0.94$	0.35
BARS global clinical assessment score change, mean (s.d.) (PP)	0.1 (0.7)	-0.2 (0.4)	$z=-0.93$	0.35
BARS global clinical assessment score change, mean (s.d.) (ITT)	0.1 (0.6)	-0.3 (0.6)	$z=-1.52$	0.13
AIMS total score change (1-7 items), mean (s.d.) (PP)	0.5 (0.5)	0.3 (0.6)	$z=-0.78$	0.44
AIMS total score change (1-7 items), mean (s.d.) (ITT)	0.4 (0.5)	0.2 (0.5)	$z=-0.95$	0.34
Rescue drugs				
Lorazepam user, n (%)	4 (30.8%)	9 (56.3%)	$\chi^2(1)=1.88$	0.17
Lorazepam dose among users, mg/day, mean (s.d.)	0.3 (0.5)	0.4 (0.6)	$z=-1.18$	0.24
Zolpidem user, n (%)	4 (30.8%)	10 (62.5%)	$\chi^2(1)=2.89$	0.09
Zolpidem dose among users, mg/day, mean (s.d.)	1.4 (2.8)	3.3 (3.2)	$z=-1.76$	0.08
Biperiden user, n (%)	0 (0.0%)	0 (0.0%)	n.a.	1.00 ^a

^a. Fisher's exact test.

PANSS, Positive and Negative Syndrome Scale; s.d., standard deviation; PP, per-protocol; ITT, intention-to-treat; CGI-GI, Clinical Global Impression-Global Improvement; GAF, Global Assessment of Functioning; SAS, Simpson-Angus Scale; BARS, Barnes Akathisia Rating Scale; AIMS, Abnormal Involuntary Movement Scale; n.a., not available