BJPsych
The British Journal of Psychiatry (2008)
193, 279–288. doi: 10.1192/bjp.bp.108.050088

Table DS1 Movement disorder characteristics at baseline

All treated patients[a]	Olanzapine All (*n*=330)	Olanzapine Excluding Phase 1a[g] (*n*=265)	Perphenazine All (*n*=257)	Quetiapine All (*n*=329)	Quetiapine Excluding Phase 1a[g] (*n*=263)	Risperidone All (*n*=333)	Risperidone Excluding Phase 1a[g] (*n*=270)	Ziprasidone All (*n*=182)[h]	Ziprasidone Excluding Phase 1a[g] (*n*=151)
Parkinsonism									
Simpson–Angus Scale EPS score: mean (s.d.)	0.21 (0.32)	0.16 (0.28)	0.19 (0.32)	0.22 (0.33)	0.16 (0.25)	0.23 (0.30)	0.20 (0.29)	0.23 (0.36)	0.17 (0.29)
Met criteria for parkinsonism,[b] *n* (%)	115 (35)	77 (29)	92 (36)	130 (40)	86 (33)	124 (37)	88 (33)	69 (38)	50 (33)
Akathisia									
BARS global clinical assessment score:[c] mean (s.d.)	0.63 (1.01)	0.58 (0.97)	0.44 (0.80)	0.47 (0.81)	0.40 (0.75)	0.58 (0.88)	0.47 (0.81)	0.55 (0.83)	0.47 (0.77)
Met criteria for akathisia,[d] *n* (%)	75 (23)	52 (20)	44 (17)	64 (19)	46 (17)	66 (20)	42 (16)	36 (20)	26 (17)
Tardive dyskinesia[e]									
AIMS total score: mean (s.d.)	1.8 (3.3)	0.8 (1.9)	0.7 (1.6)	1.9 (3.4)	0.7 (1.5)	1.8 (3.2)	0.7 (1.5)	1.8 (3.2)	0.8 (1.6)
Met modified Schooler–Kane criteria,[f] *n* (%)	54 (16)	14 (5)	12 (5)	61 (19)	12 (5)	52 (16)	5 (2)	28 (15)	5 (3)
Met criteria for borderline tardive dyskinesia,[f] *n* (%)	48 (15)	23 (9)	16 (6)	34 (10)	17 (6)	40 (12)	24 (9)	20 (11)	11 (7)
No tardive dyskinesia,[f] n (%)	228 (69)	228 (86)	229 (89)	234 (71)	234 (89)	241 (72)	241 (89)	134 (73)	134 (89)

AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; EPS, extrapyramidal side-effects.
a. Patients who took at least one dose of randomised study medication.
b. Patients met criteria for parkinsonism at baseline based on Simpson–Angus Scale EPS criteria (2 items rated as mild (=1) or 1 item rated as moderate (=2)) or were taking medications for parkinsonism.
c. Overall treatment group differences in BARS global clinical assessment for all patients from ANOVA *F*-test *P*=0.042. Olanzapine is larger than perphenazine.
d. Patients met criteria for akathisia at baseline based on BARS global clinical assessment of at least mild (=2) or were taking medications for akathisia.
e. Overall treatment group differences in AIMS score for all patients from ANOVA *F*-test *P*<0.001. Perphenazine is smaller than all other treatments. Overall treatment group differences in tardive dyskinesia criteria categories for all patients from chi-squared test *P*<0.001. Perphenazine has fewer tardive dyskinesia events than all other treatments.
f. Patients met modified Schooler–Kane criteria for tardive dyskinesia based on AIMS scale criteria (2 items rated as mild (=2) or 1 item rates as moderate(=3)). Patients met criteria for borderline tardive dyskinesia if they did not meet modified Schooler–Kane criteria, but did meet at least one of the following: stratified into Phase 1a, taking medications identified by the principal investigator as taken for tardive dyskinesia, reported history of tardive dyskinesia, or a score of mild (=2) on one AIMS item. Patients with no tardive dyskinesia at baseline met none of the criteria for modified Schooler–Kane tardive dyskinesia or borderline tardive dyskinesia.
g. Phase1a patients were excluded from randomisation that included perphenazine. Patients were stratified into Phase1a based on the principal investigator's assessment of tardive dyskinesia or a past history of tardive dyskinesia.
h. Baseline movement disorder status of one patient on ziprasidone could not be determined owing to insufficient data, so number of patients is reduced from 183 to 182.

Table DS2 Observed parkinsonism events for people with no parkinsonism at baseline[a]

	Olanzapine	Perphenazine	Quetiapine	Risperidone	Ziprasidone
All eligible patients, *n*	215	165	199	209	113
Any parkinsonism event,[b] *n*/*N*[c] (%)	70/201 (34.8)	48/160 (30.0)	55/187 (29.4)	71/191 (37.2)	31/98 (31.6)
Met Simpson–Angus Scale EPS criteria,[d] *n*/*N*[c] (%)	64/201 (31.8)	45/160 (28.1)	53/187 (28.3)	62/191 (32.5)	28/98 (28.6)
Discontinued for parkinsonism events, *n* (%)	8 (3.7)	5 (3.0)	0	4 (1.9)	0
Added medications for parkinsonism, *n* (%)	10 (4.7)	7 (4.2)	2 (1.0)	14 (6.7)	4 (3.5)

EPS, extrapyramidal side-effects.
a. Patients with no parkinsonism at baseline did not meet Simpson–Angus Scale EPS criteria and were taking no medications for parkinsonism at baseline.
b. A parkinsonism event includes meeting Simpson–Angus scale EPS criteria, discontinuing due to parkinsonism, or adding medications for parkinsonism
c. *n*=number of events, *N*=number of patients with non-missing outcome.
d. Patients met Simpson–Angus Scale EPS criteria if they had two items rated as mild (=1) or one item rated as moderate (=2).

Table DS3 Observed akathisia events for people with no akathisia at baseline[a]

	Olanzapine	Perphenazine	Quetiapine	Risperidone	Ziprasidone
All eligible patients, *n*	255	213	265	267	146
Any akathisia event,[b] *n*/*N*[c] (%)	52/238 (22)	51/207 (25)	42/250 (17)	61/244 (25)	26/130 (20)
Met BARS global assessment criteria,[d] *n*/*N*[c] (%)	46/238 (19)	42/206 (20)	38/250 (15)	55/244 (23)	25/130 (19)
Discontinued for akathisia, *n* (%)	5 (2)	10 (5)	3 (1)	6 (2)	4 (3)
Added medications for akathisia, *n* (%)	9 (4)	17 (8)	6 (2)	16 (6)	4 (3)

BARS, Barnes Akathisia Rating Scale.
a. Patients with no akathisia at baseline had a BARS global clinical assessment of less than mild (=2) and were taking no medications for parkinsonism at baseline.
b. An akathisia event includes meeting BARS global assessment criteria, discontinuing due to akathisia, or adding medications for akathisia.
c. *n*=number of events, *N*=number of patients with non-missing outcome.
d. Patients met BARS global clinical assessment criteria if they had a score of at least mild (=2).

Table DS4 Observed tardive dyskinesia events for people with no tardive dyskinesia at baseline[a]

	Olanzapine	Perphenazine	Quetiapine	Risperidone	Ziprasidone
All eligible patients, *n*	228	229	234	241	134
Schooler–Kane criteria, *n*/*N*[b] (%)	2/182 (1.1)	6/183 (3.3)	8/179 (4.5)	4/179 (2.2)	3/89 (3.3)
Modified Schooler–Kane criteria,[c] *n*/*N*[b] (%)	20/216 (9.3)	26/221 (11.8)	19/222 (8.6)	21/220 (9.6)	10/120 (8.3)
Discontinued for tardive dyskinesia, *n* (%)	0	2 (1)	1 (<1)	0	0
Added medications for tardive dyskinesia, *n* (%)	1 (<1)	0	1 (<1)	2 (1)	0

a. Patients with no tardive dyskinesia at baseline met none of the criteria for modified Schooler–Kane tardive dyskinesia or borderline tardive dyskinesia.
b. *n*=number of events, *N*=number of patients with non-missing outcome (Schooler–Kane tardive dyskinesia criteria required on at least two consecutive post-baseline Abnormal Involuntary Movement Scale assessments).
c. Schooler–Kane criteria required on only one post-baseline Abnormal Involuntary Movement Scale assessment.

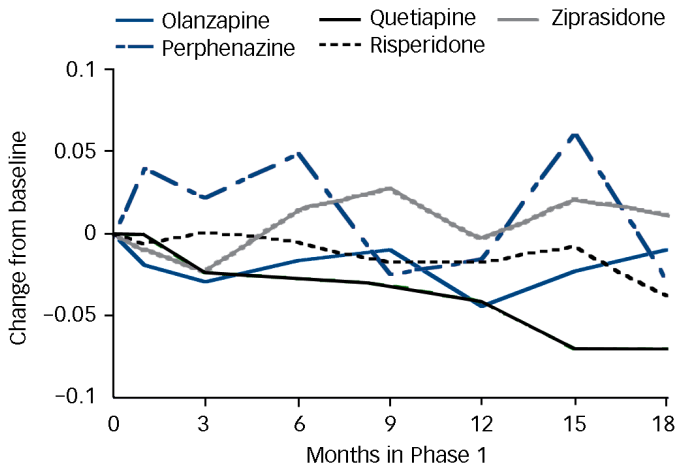

Fig. DS1 Mixed model least squares mean estimated change in Simpson–Angus Scale mean score over time.[a]

a. Adjusted for covariates, for all patients. *P*=0.101 for overall four treatment group comparison in analytic data-set I. The model includes fixed effects for treatment, baseline Simpson–Angus Scale score for extrapyramidal side-effects, site care setting, Phase 1a tardive dyskinesia status where applicable, classification of time, and the interaction between baseline Simpson–Angus Scale score and time. Correlations are modelled with a random intercept and spatial power covariance structure. Perphenazine estimates are from a model excluding Phase 1a tardive dyskinesia (data-set I), ziprasidone estimates are from a model with only the ziprasidone cohort patients (data-set III). Sample sizes decrease over time from month 1 to month 18 as follows: olanzapine, 308 to 124; perphenazine, 241 to 67; quetiapine, 305 to 61; risperidone, 300 to 90; ziprasidone, 161 to 40.

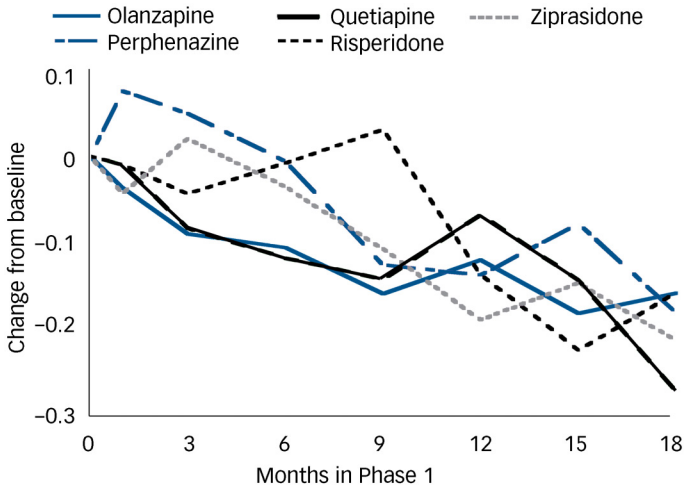

Fig. DS2 Mixed model least squares mean estimated change in Barnes Akathisia Rating Scale global clinical assessment of akathisia over time.[a]

a. Adjusted for covariates for all patients. *P*=0.294 for overall four treatment group comparison in analytic data-set I. The model includes fixed effects for treatment, baseline Barnes Akathisia Rating Scale (BARS) clinical global assessment score, age, site care setting, tardive dyskinesia status at baseline (randomised into Phase 1a) where appropriate, classification of time, and the interaction between baseline BARS global assessment and time, and treatment and time. Correlations are modelled with a random intercept and spatial power covariance structure. Perphenazine estimates are from a model excluding Phase 1a tardive dyskinesia (data-set I), ziprasidone estimates are from a model with only the ziprasidone cohort patients (data-set III). Sample sizes decrease over time from month 1 to month 18 as follows: olanzapine, 309 to 124; perphenazine, 242 to 67; quetiapine, 305 to 61; risperidone, 300 to 90; ziprasidone 163 to 40.

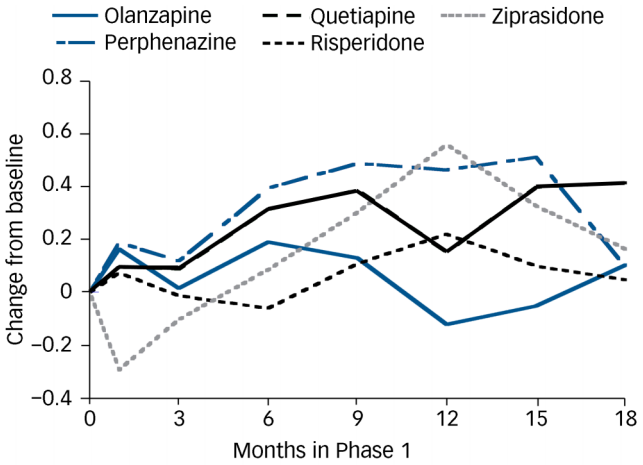

Fig. DS3 Mixed model least squares mean estimated change in Abnormal Involuntary Movement Scale total score over time.[a]

a. Adjusted for covariates, excluding patients randomised to Phase 1a. *P*=0.351 for overall four treatment group comparison in data-set I. The model includes fixed effects for treatment, baseline Abnormal Involuntary Movement Scale (AIMS) score, age category (<25, 25–29, 30–39, 40–49, 50+), classification of time, the interaction between baseline AIMS score and time, and treatment and time. Correlations are modelled with a random intercept and spatial power covariance structure. Ziprasidone estimates are from a model with only the ziprasidone cohort patients (data-set III). Sample sizes decrease over time from month 1 to month 18 as follows: olanzapine, 247 to 97; perphenazine, 241 to 67; quetiapine, 246 to 51, risperidone, 245 to 80; ziprasidone, 134 to 31. Phase 1a patients were excluded from randomisation to perphenazine. Patients were stratified into Phase 1a based on the principal investigator's assessment of tardive dyskinesia or a history of tardive dyskinesia.