Quetiapine, A Novel Antipsychotic: Experience in Elderly Patients With Psychotic Disorders

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Background: This uncontrolled trial examines the safety and effects of quetiapine, a new atypical antipsychotic, in elderly patients with psychotic disorders.

Method: This is an ongoing, multicenter, open-label, 52-week trial of quetiapine in men and women at least 65 years old with DSM-IV psychotic disorders. Patients received quetiapine, 25 to 800 mg/day. Assessments included the 18-item Brief Psychiatric Rating Scale (BPRS), the Clinical Global Impressions scale (CGI), the Simpson-Angus Neurologic Rating Scale, and the Abnormal Involuntary Movement Scale (AIMS).

Results: An interim analysis was performed at 12 weeks with results from 151 patients. The median total daily dose was 100 mg/day. The most common adverse events were somnolence (32%), dizziness (14%), postural hypotension (13%), and agitation (11%). Extrapyramidal symptom adverse events occurred in 6% of patients. Mean Simpson-Angus Scale total score showed significant ($p < .0001$) improvement at endpoint; there were no changes in AIMS scores. BPRS total and CGI-Severity of Illness scores showed significant ($p < .0001$ and $p < .01$, respectively) improvement at endpoint. No clinically important effects were reported for hematologic or liver function test variables; small changes in mean free levorotatory thyroxine (T_4) levels were not associated with substantial changes in mean thyroid-stimulating hormone concentration. Mean corrected QT interval (QTc) was unchanged, but a slight increase in mean heart rate was noted.

Conclusion: Quetiapine was well tolerated in a nonrandomized study of elderly patients and was associated with improvement in symptoms.

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As the elderly segment of the population continues to grow, the number of elderly patients with psychiatric illnesses is likely to grow as well.[1] In the elderly, the prevalence of various types of depression, anxiety, dementia, and psychotic disorders can be as high as 10% for noninstitutionalized persons and 50% for nursing home residents.[2] For institutionalized patients, antipsychotics are the most widely prescribed psychotropic drugs,[3] yet special consideration is required when prescribing these drugs to elderly patients.[4]

Physiologic changes related to aging can alter the pharmacokinetic and pharmacodynamic characteristics of antipsychotic agents, making the elderly more vulnerable than younger adults to the adverse side effects associated with these drugs.[5] Baroreceptor sensitivity and venous tone are reduced in the elderly, making them more susceptible to orthostatic hypotension, which can lead to falls, fractures, and other injuries.[6] In addition to orthostatic hypotension, the cardiovascular effects of standard antipsychotics include tachycardia (as a secondary response to orthostatic hypotension and cholinergic blockade), nonspecific T wave changes, and QT interval prolongation.[7] Therefore, low-potency antipsychotics (e.g., chlorpromazine, thioridazine), whose side effects include orthostatic hypotension as well as sedation and anticholinergic side effects (e.g., dry mouth, blurred vision, urinary retention, constipation), are not recommended for elderly patients.[7] Higher potency antipsychotics (e.g., haloperidol, fluphenazine) are generally preferred for older patients with psychotic disorders,[7] but are associated with extrapyramidal symptoms (EPS) and tardive dyskinesia, which can reduce the benefit-to-risk ratio of these agents[8]; old age is a risk factor for the development of tardive dyskinesia,[9] and age affects both the prevalence and the severity of the condition.[8] In addition, the elderly are particularly vulner-

able to developing parkinsonism,[10] and the drugs used to treat EPS are also associated with unwanted anticholinergic side effects.[8]

Atypical antipsychotic agents, such as clozapine, have shown promise because of their apparent lack of EPS; however, they may present other problems for the elderly.[8] Among the adverse effects associated with clozapine (e.g., sedation, anticholinergic effects),[11] the incidences of agranulocytosis and delirium appear to increase with age.[12,13] The cardiac effects of clozapine (e.g., orthostatic hypotension, tachycardia, arrhythmias) can also limit its use in older patients.[8] Risperidone, a relatively new antipsychotic agent, produces fewer EPS than haloperidol; however, its potential for producing EPS appears to be dose related.[14] Olanzapine, another recently introduced antipsychotic, also produces fewer EPS than haloperidol; however, treatment-emergent parkinsonism occurred with olanzapine (12.5–17.5 mg/day) at approximately one third the rate with haloperidol.[15]

Quetiapine is a new dibenzothiazepine derivative that has a novel pharmacologic profile. Quetiapine has a higher affinity for serotonin 5-HT_{2A} receptors (IC_{50} = 148 nM) than for dopamine D_2 receptors (IC_{50} = 329 nM).[16] Preclinical tests predictive of EPS indicated that quetiapine would have a low EPS liability. Quetiapine demonstrated selectivity for the limbic system by producing depolarization blockade of the A10 mesolimbic but not the A9 nigrostriatal dopamine-containing neurons after chronic administration.[17] At effective dopamine D_2 receptor–blocking doses, quetiapine produced only weak catalepsy and exhibited minimal dystonic liability in haloperidol-sensitized or drug-naive cebus monkeys after acute and chronic administration.[18] These findings suggested that quetiapine would be effective in treating the symptoms of schizophrenia and would also be well tolerated.

Results from placebo-controlled clinical trials supported the preclinical findings and have shown quetiapine to be effective in improving the symptoms of schizophrenia across the therapeutic dose range (150–750 mg/day); improvement was seen in both positive and negative symptoms.[19,20] In trials controlled with standard antipsychotic agents, quetiapine was as effective as haloperidol or chlorpromazine in improving psychotic symptoms.[20,21] Quetiapine was well tolerated, and the most common side effects included sedation and somnolence, which usually occurred during the titration phase of treatment initiation.[22] Quetiapine had no clinically important effects on hematology, electrocardiograms, or vital signs variables[23]; there were no statistically significant differences in the proportion of patients who experienced changes in corrected QT interval (QTc) following treatment with quetiapine or placebo.[20,24] The incidence of EPS and the use of anticholinergic medications with quetiapine was no different than with placebo across the therapeutic dose range.[20,25] In addition, quetiapine did not produce sustained increases in plasma prolactin concentrations (across the therapeutic dose range) and was not associated with side effects related to elevated plasma prolactin concentrations, such as gynecomastia, galactorrhea, amenorrhea, and impotence.[20,26]

Table 1. DSM-IV Psychotic Disorders Qualifying Patients for Trial Entry

Idiopathic psychoses
Schizophrenia
Schizophreniform disorder
Schizoaffective disorder
Delusional disorder
Shared psychotic disorder
Major depressive disorder
Bipolar disorder
Organic psychoses
Dementia
Alzheimer's type
Vascular
Due to head trauma
Due to Pick's disease
Due to Parkinson's disease
Psychotic disorder due to Parkinson's disease

A preliminary pharmacokinetic and safety trial of quetiapine in elderly patients with psychotic disorders showed that quetiapine was well tolerated in this population, with no major safety concerns arising.[27] This trial also showed that quetiapine clearance was 30% to 50% lower in the elderly than in younger adults.[28] We report here safety and effects on psychotic symptoms of quetiapine from an ongoing, open-label trial in elderly patients.

METHOD

Patients

Men and women aged 65 years or older (or ≥ 50 years for patients with a concomitant diagnosis of Parkinson's disease) referred by clinical and medical staff or by physicians, were eligible for trial entry if they met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV)[29] criteria for any of the disorders listed in Table 1.

In addition, patients who had active, chronic, or recurrent psychotic symptoms severe enough to require antipsychotic medication were eligible for inclusion in the trial. Patients who met DSM-IV diagnostic criteria for any other psychiatric disorder coded on Axis I were excluded. Conditions likely to interfere with safety evaluations, such as clinically significant laboratory findings or abnormal electrocardiograms, were also reasons for exclusion.

Patients eligible for trial entry were hospitalized, resided in domiciliary facilities (such as nursing or group homes), or lived in private homes with the supervision of a reliable family member or a sponsor. Institutional review board approval was granted for the clinical research facility, and written informed consent was given before trial entry by the patient, spouse, parent, or legal guardian.

Trial Design

This was a multicenter, open-label, 52-week trial. The trial was divided into 2 segments to provide an interim point for data analysis. The duration of segment A was 12 weeks (week 0 to week 12) and the duration of segment B was 40 weeks (week 13 to week 52). Because this is an ongoing trial, only data from segment A are presented.

Patients were to begin quetiapine with a 25-mg dose, given once or twice daily, as tolerated. Doses were escalated in 25-mg to 50-mg increments every 1 to 3 days, up to 800 mg/day, according to the patient's tolerance and clinical response. All antipsychotic medications and medications for the treatment of EPS were withdrawn at the beginning of segment A. No concurrent antipsychotic medications were allowed during the trial. Psychotropic medications, other than antipsychotic medications, received before the start of segment A were allowed to continue at the same dose through week 4. New psychotropic medications, other than those required for treating agitation and insomnia, were not allowed before the completion of the week 4 assessments. Chloral hydrate was permitted orally throughout the trial for acute agitation or severe insomnia, up to 2000 mg in 24 hours. Patients unresponsive to chloral hydrate could receive lorazepam (2 mg, p.o. or i.m.), up to 6 mg in 24 hours, but not within 12 hours before psychiatric or neurologic assessments. Benztropine mesylate was permitted as needed for the treatment of EPS.

Safety Assessments

Adverse events were assessed by the investigator throughout the trial for severity and relationship to treatment. EPS and abnormal involuntary movements were assessed using the Simpson-Angus Neurologic Rating Scale,[30] modified to include an akathisia item, and the Abnormal Involuntary Movement Scale (AIMS),[31] respectively, at entry and at weeks 2, 4, 8, and 12. Additional safety measures, assessed at screening and throughout the trial, included hematology, liver function tests (LFTs), and electrocardiography (ECG) (weeks 1, 2, 4, 8, and 12); thyroid function tests, clinical chemistry, and urinalysis (weeks 4 and 12); vital signs measurements (twice weekly until week 4 and at weeks 6, 8, 10, 12); and weight measurement and complete physical examinations (week 12). Patients who withdrew before completing the trial were to complete all assessments on the day of withdrawal.

Clinical Measures

Although designed primarily as a safety and tolerability trial, changes in psychiatric symptomatology were assessed using the 18-item Brief Psychiatric Rating Scale (BPRS; 0–6 scoring [0 = not present, 6 = extremely severe])[32] and the Clinical Global Impressions scale (CGI).[33] Both assessments were performed at week 0 (baseline) and at weeks 2, 4, 8, and 12. Patients who withdrew before completing the trial were to complete all assessments on the day of withdrawal. Response rates at endpoint were defined as the proportions of patients with a decrease from baseline in BPRS total score of 20%, 40%, 60%, and 80%.

Statistical Analyses

Week 12 was considered the endpoint for this interim analysis. All patients who received active treatment were included in safety analyses. Descriptive statistics (N, mean, standard deviation, minimum, maximum) for total daily dose at treatment endpoint were calculated and presented according to subpopulation (idiopathic or organic). Medications used for the treatment of agitation, insomnia, and EPS during active treatment were recorded. Concomitant medications of interest included chloral hydrate and lorazepam (for agitation and insomnia), and benztropine mesylate (for EPS).

Data from patients who had Simpson-Angus Scale, AIMS, BPRS, and CGI assessments both at baseline and at one or more time points after baseline were analyzed for changes from baseline. Patients who withdrew before week 12 had data from their last observations carried forward (LOCF) included with endpoint data; therefore, endpoint data include both observed week-12 data and LOCF data. Data were grouped according to the 2 subpopulations and summarized for all patients. Descriptive statistics were calculated for each assessment. Changes from baseline at endpoint for Simpson-Angus Scale and AIMS total scores were analyzed using the Wilcoxon rank sum test for matched pairs. For BPRS total and CGI-Severity of Illness (CGI-S) scores, changes from baseline were analyzed using a paired t test.

Occurrences of deaths, withdrawals due to adverse events, and other adverse events during active treatment were recorded. Adverse events were tabulated by preferred term using the COSTART (FDA Coding Symbols for Thesaurus of Adverse Reaction Terms) system of nomenclature. Numbers and crude incidence rates of all adverse events during active treatment were summarized by COSTART body system and preferred term.

Descriptive statistics were calculated for mean and change from baseline for hematology, clinical chemistry, and urinalysis test results; for ECG parameters (atrial and ventricular rates; PR, QRS, and QT intervals; and QTc); and for vital signs. Changes from baseline at endpoint were compared using paired t tests. Frequencies of protocol-defined clinically significant values for selected laboratory tests were also recorded.

RESULTS

Patients

Demographic details and DSM-IV diagnoses are provided in Table 2. A majority of the 151 patients entered in

Table 2. Demographic Details and Diagnoses

Variable	Value
Patients enrolled and received trial medication, N (%)	151 (100)
Age, y, mean (range)	76.8 (62–94)
Weight, kg, mean (range)	65.6 (34–120)
Race, N (%)	
White	131 (87)
Other	20 (13)
Sex, N (%)	
Women	86 (57)
Men	65 (43)
DSM-IV diagnosis, N (%)	
Idiopathic	45 (30)
Schizophrenia	
Paranoid	15 (10)
Undifferentiated	10 (7)
Disorganized	1 (1)
Residual	1 (1)
Delusional disorder	7 (5)
Schizoaffective disorder	6 (4)
Bipolar disorder	4 (3)
Major depressive disorder	1 (1)
Organic	106 (70)
Dementia	
Due to Alzheimer's disease	75 (50)
Due to Parkinson's disease or head trauma	3 (2)
Vascular	11 (7)
Psychotic disorder due to Parkinson's disease	17 (11)

the trial were white (87%) and were women (57%); the mean age was 77 years. Most patients were diagnosed with organic psychotic disorders (70%). Psychoses were associated with Alzheimer's disease (N = 75), schizophrenia (N = 27), Parkinson's disease (N = 20), vascular dementia (N = 11), delusional disorder (N = 7), schizoaffective disorder (N = 6), bipolar disorder (N = 4), and major depressive disorder (N = 1). Thirty-six patients (24%) withdrew from the trial: 13 withdrew because of adverse events, 12 refused to continue or were lost to follow-up, 9 withdrew because of lack of effect, and 2 withdrew because of protocol noncompliance.

Exposure

The mean duration of exposure to quetiapine was 73 days (range, 2–87 days). The median total daily dose was 100 mg/day (range, 13–400 mg/day) and was similar for patients with idiopathic (median = 75 mg/day; range, 25–400 mg/day) and organic (median = 100 mg/day; range, 13–375 mg/day) psychoses.

Concomitant medication to treat EPS was used in 17 patients (11%) for short durations (usually 3 days or less); 13 patients received benztropine mesylate, 3 received trihexyphenidyl, and 1 received amantadine.

Adverse Events

The most common adverse events were somnolence, dizziness, postural hypotension, and agitation (Table 3). Accidental injury (e.g., fall, fracture, laceration) occurred in 12% of patients but was not attributed to quetiapine in any patient. Two patients died after having pneumonia; both cases were unrelated to treatment with quetiapine. Thirteen patients (9%) withdrew due to adverse events; adverse events leading to withdrawal that occurred in 2 or more patients were somnolence (3 patients), dizziness (2 patients; in 1 case, associated with hypotension), and pneumonia (2 patients). One patient withdrew because of QT interval prolongation.

EPS adverse events occurred in 9 patients (6%), and consisted of akathisia (5 patients), tremor (2 patients), neck rigidity (1 patient), and extrapyramidal syndrome (1 patient); no dystonia was noted. All EPS adverse events were rated as mild except for 1 case of akathisia rated as moderate. Anticholinergic adverse events consisted of constipation and dry mouth and were reported in 12 patients (8%) and 6 patients (4%), respectively; most cases were mild.

Table 3. Adverse Events[a]

	Patients With Adverse Event		Intensity,[b] N		
Adverse Event	N	%	Mild	Moderate	Severe
Somnolence	48	32	33	11	4
Dizziness	21	14	15	6	0
Postural hypotension	19	13	18	0	1
Accidental injury[c]	18	12	6	12	0
Agitation	16	11	1	11	4
Constipation	12	8	8	4	0
Headache	11	7	10	1	0
Electrocardiogram abnormal	10	7	9	0	1
Insomnia	9	6	5	3	1
Urinary tract infection	9	6	6	3	0
Hypotension	8	5	6	2	0
Diarrhea	7	5	5	1	1

[a]Occurring in at least 5% of patients.
[b]As assessed by investigator.
[c]Not attributable to quetiapine.

Table 4. Neurologic Rating Scale Scores (Mean ± SD)[a]

Scale	Baseline	Endpoint	Δ From Baseline	p Value[b]
Simpson-Angus Scale total				
Idiopathic	19.4 ± 7.1	16.8 ± 5.8	–2.7 ± 4.7	.0007
Organic	17.5 ± 6.7	15.8 ± 5.3	–1.8 ± 3.8	.0001
All	18.1 ± 6.8	16.1 ± 5.5	–2.1 ± 4.1	.0001
AIMS total				
Idiopathic	8.9 ± 7.4	8.7 ± 7.3	–.3 ± 5.3	.7103
Organic	2.8 ± 5.3	3.1 ± 5.4	.3 ± 3.4	.2960
All	4.7 ± 6.6	4.8 ± 6.6	.1 ± 4.1	.6201

[a]Abbreviation: AIMS = Abnormal Involuntary Movement Scale.
[b]Wilcoxon rank sum test for matched pairs, change from baseline at endpoint.

Neurologic Rating Scales

Simpson-Angus Scale total scores demonstrated a small but statistically significant improvement at endpoint (Table 4). The mean Simpson-Angus Scale total score at baseline was 18.1 (range, 10–38; no EPS = 10). At the final assessment, the mean Simpson-Angus Scale

total score was 16.1 (range, 10–33); the change from baseline of –2.1 (range, –17 to 6) was statistically significant ($p < .0001$). No statistically significant changes were seen in mean AIMS total scores. At baseline, mean AIMS total score was 4.7 (range, 0–29; no abnormal involuntary movements = 0). At endpoint, the AIMS mean total score was 4.8 (range, 0–26); the change from baseline was 0.1 (range, –15 to 15).

Clinical Laboratory Tests

Mean hematologic values were within normal limits throughout the trial. At endpoint, mean white blood cell count was 6.79×10^9/L (range, 3.50×10^9/L to 14.40×10^9/L) and mean absolute neutrophil count was 4.35×10^9/L (range, 1.15×10^9/L to 12.23×10^9/L).

Mean changes from baseline in LFTs throughout the trial were small and clinically unimportant. At endpoint, small mean changes were noted in alanine aminotransferase (ALT; +0.05 U/L; normal range, 0–48 U/L), aspartate aminotransferase (AST; –0.34 U/L; normal range, 0–53 U/L), total bilirubin (+0.11 μmol/L; normal range, 5.1–25.7 μmol/L), and alkaline phosphatase (+7.39 U/L; normal range, 15–110 U/L). One patient, who entered the trial with high but not clinically significant LFT values, had clinically significant (3 × upper limit of normal) LFT values during the trial; the maximum ALT and AST values for this patient were 150 U/L and 168 U/L, respectively, and were the highest ALT and AST values reported during the trial. At endpoint, these LFT values remained elevated, but were improving.

A small decrease from baseline in mean free levorotatory thyronine (T_4) was noted at endpoint (–1.72 pmol/L; normal range, 15.4–29.6 pmol/L). However, the decrease in free T_4 was not associated with an increase in thyrotropin concentration (decrease from baseline at endpoint = –0.53 μU/L; normal range, 0.4–5.5 μU/L).

Electrocardiography

No clinically important changes from baseline were noted in ECG rates or intervals. Small increases from baseline in mean atrial (+3.14 b.p.m.) and ventricular (+2.48 b.p.m.) rates were noted at endpoint. Mean changes from baseline at endpoint in QTc and in PR and QT intervals were 0.000, 0.000, and –0.006 seconds, respectively.

Vital Signs and Weight

In general, small decreases were noted for supine and standing systolic blood pressure (mean change from baseline = –1.27 mm Hg and – 3.60 mm Hg, respectively), and small increases were noted for supine and standing pulse (mean change from baseline = +1.75 b.p.m. and +2.89 b.p.m., respectively). Clinically significant changes in postural systolic blood pressure (decrease of 30 mm Hg or more from supine to standing position) and pulse (increase of 20 b.p.m. or more from supine to standing position) were reported in 23% and 27% of patients, respectively; however, only 5% reported postural changes in both systolic pressure and pulse.

Overall, there was no mean weight gain during this trial. The mean change from baseline at endpoint in weight was +0.78 kg. Nine patients (6%) had clinically significant increases in weight (increase from baseline of 7% or greater).

Table 5. BPRS Total and CGI-S Scores (Mean ± SD)[a]

Scale	Baseline	Endpoint	Δ From Baseline	p Value[b]
BPRS total				
Idiopathic	29.2 ± 15.1	24.4 ± 15.4	–4.7 ± 11.4	.0105
Organic	28.6 ± 13.1	22.6 ± 12.5	–6.0 ± 11.0	< .0001
All	28.8 ± 13.7	23.2 ± 13.4	–5.6 ± 11.1	< .0001
CGI-S				
Idiopathic	4.2 ± 1.1	3.8 ± 1.2	–.4 ± 1.0	.0165
Organic	4.2 ± 1.0	4.0 ± 1.1	–.2 ± 1.0	.1172
All	4.2 ± 1.0	4.0 ± 1.1	–.2 ± 1.0	.0085

[a]Abbreviations: BPRS = Brief Psychiatric Rating Scale, CGI-S = Clinical Global Impressions-Severity of Illness scale.
[b]Paired t test, change from baseline at endpoint.

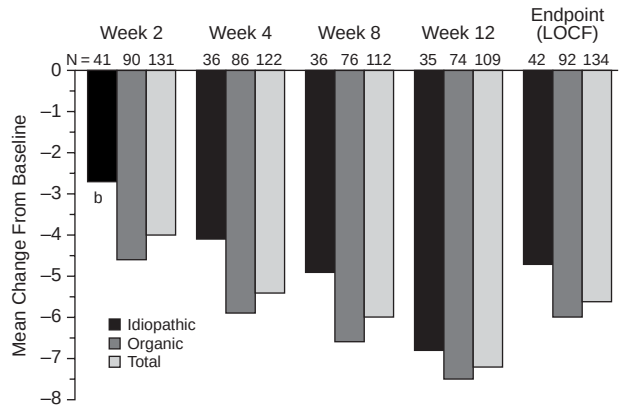
Clinical Measures

Of the 151 patients who entered this trial, 134 had efficacy assessments at baseline and at least 1 postbaseline assessment. BPRS total score and CGI-S score improved progressively during the course of the trial. Decreases from baseline for both assessments were significant ($p < .01$) at all time points measured (weeks 2, 4, 8, and 12) and at endpoint when all patients were assessed (Table 5). Assessing the data separately for the 2 subpopulations showed that the degree of improvement for patients diagnosed with idiopathic and those with organic psychoses was comparable (Figures 1 and 2). Mean CGI-Global Improvement scores ranged from 2.8 to 3.3 at the timepoints sampled (weeks 2, 4, 8, and 12; a score of 3 = minimally improved). Overall, 52% of all patients had at least a 20% decrease from baseline in BPRS total score at endpoint (Figure 3); the percentages of patients responding in the 2 subpopulations were similar (48% with idiopathic and 54% with organic psychoses).

DISCUSSION

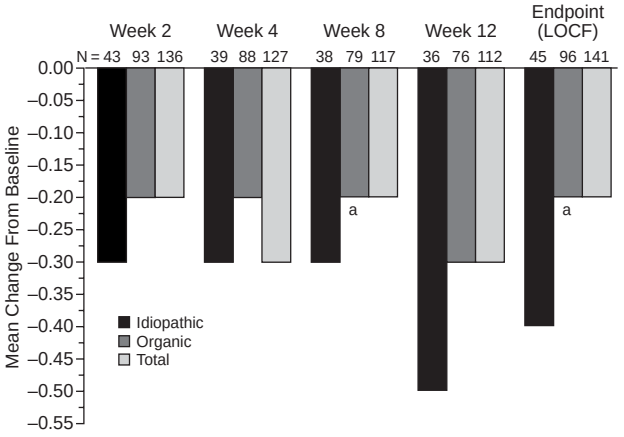
The results of this open-label trial showed quetiapine to be well tolerated by elderly patients with psychotic symptoms. Although this uncontrolled trial was not designed to definitively establish clinical efficacy, improvement was observed in the BPRS total and CGI-S scores. Efficacy results were comparable between patients with idiopathic psychoses and those with organic psychoses; baseline mean BPRS and CGI-S scores showed that both patient subpopulations were equally ill at trial entry.

Figure 1. Mean Change From Baseline in BPRS Total Score at Weeks 2, 4, 8, and 12 and Endpoint[a]



[a]Abbreviation: LOCF = last observation carried forward.
[b]Decrease from baseline not statistically significant.

Figure 2. Mean Change From Baseline in CGI-S Score at Weeks 2, 4, 8, and 12 and Endpoint

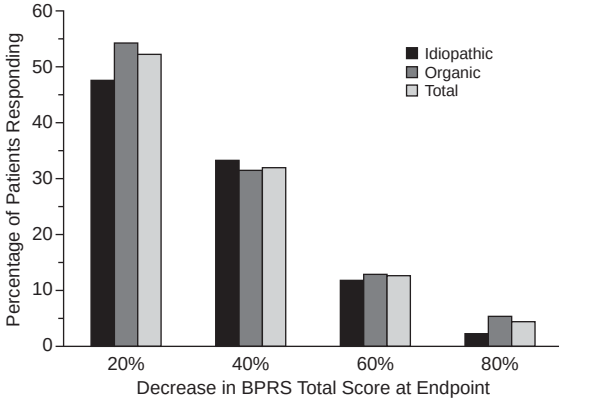


[a]Decrease from baseline not statistically significant.

Patients with idiopathic psychoses and those with organic psychoses received similar doses of quetiapine (median daily doses were 75 mg and 150 mg, respectively). However, quetiapine doses used in this elderly population were 40% to 80% lower than those used in younger patient populations, which were in the range of 150 to 750 mg/day.[20] Previous pharmacokinetic trials have shown that elderly psychotic patients have reduced oral clearance of quetiapine compared with younger psychotic patients and may require smaller doses.[27,28]

Quetiapine was well tolerated in this elderly population. The most common side effects were related to the central nervous system (somnolence) and the cardiovascular system (dizziness and postural hypotension). These results agree with the adverse event profile of quetiapine in younger patients and with the increased sensitivity of the elderly to antipsychotic agents. Symptoms of the underlying illness may have also been reported as adverse events (agitation, insomnia). Few patients had anticholinergic side effects (4% dry mouth and 8% constipation). Most of the adverse events reported were considered mild or moderate and are common to this class of drug.

Figure 3. Summary of Response Rates at Endpoint



Quetiapine was associated with negligible EPS, as demonstrated across a number of outcome measures. Simpson-Angus Scale total scores actually improved significantly during the course of the trial, suggesting resolution of side effects from typical antipsychotics used before trial entry. This improvement was similar to that seen in previous placebo-controlled trials of quetiapine in younger patients.[20] EPS adverse events occurred infrequently (6% of patients) and at a lower rate than in younger patients receiving placebo in previous controlled quetiapine trials, where total EPS for quetiapine and placebo were 7% and 12%, respectively.[34] Concomitant anticholinergic medication use was limited and usually used for short durations (3 days or less).

Quetiapine had no clinically important effects on hematologic or LFT variables in this patient population. Small changes in mean free T_4 levels were not associated with substantial changes in mean thyroid-stimulating hormone levels, similar to findings in younger adults.[20] Quetiapine was not associated with QTc prolongation, but did appear to produce a slight increase in heart rate. Quetiapine was rarely associated with weight gain in this population.

Quetiapine is well tolerated in the older patient. The favorable safety results and improvement in psychotic symptoms from this nonrandomized trial support further controlled clinical trials of quetiapine in the elderly.

Drug names: amantadine (Symmetrel), benztropine (Cogentin and others), chloral hydrate (Noctec), chlorpromazine (Thorazine and others), clozapine (Clozaril), fluphenazine (Prolixin and others), haloperidol (Haldol and others), lorazepam (Ativan and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), thioridazine (Mellaril and others), trihexyphenidyl (Artane and others).

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