= 100) were evaluated for extrapyramidal side effects (EPS) (blind) as well as other side effects and mental condition (non-blind).

Methods: Chronic schizophrenic patients were evaluated from the charts from the beginning of the present treatment (1–20 years) and prospectively for 5 years. The following rating scales were used: The Sct. Hans Rating Scale for EPS (SHRS) which includes videotape recording, Brief Psychiatric Rating Scale (BPRS), the UKU side effect scale and the Clinical Global Impression scale (CGI).

Results: There was a significantly lower prevalence of tardive dyskinesia (TD) in clozapine treated patients than control patients, although prior to this treatment there were more TD in the clozapine group ($p < 0.05$). This lower level of TD in the clozapine group was related to a lower induction of new cases ($p < 0.001$) and a tendency towards greater disappearance of TD in the clozapine group than in the control group. Clozapine treated patients without TD had started clozapine and ceased traditional neuroleptics at an earlier age than those with TD. Parkinsonian signs were seen in 33% of the clozapine treated patients versus 61% of the control patients. Psychic akathisia was found in 14% versus 40% and motor akathisia in 7% versus 29% of the patients, all differences significantly in favour of clozapine. The 5-year evaluation is going on and will be reported. Preliminary data suggest that the lower induction of new cases of TD and the tendency towards greater disappearance of TD in the clozapine treated group continues resulting in an additional decrease of TD among the clozapine treated patients.

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LONG-TERM EFFICACY, SAFETY, AND TOLERABILITY OF RISPERIDONE IN ELDERLY PSYCHOTIC PATIENTS

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A 12-month, open-label, multicenter trial of risperidone in elderly psychotic patients is being conducted. Results from 106 patients treated for 3 months (endpoint) are reported. The mean daily dose of risperidone (oral solution) at endpoint was 3.7 mg. Statistically significant improvements in psychopathology (score reductions on the Positive and Negative Syndrome Scale and the Clinical Global Impression scale) were shown by the patients at endpoint; 57% were rated as clinically improved (≥20% reduction in PANSS scores). Severity of extrapyramidal symptoms (scores on the Extrapyramidal Symptom Rating Scale) was low at baseline and was significantly reduced during treatment. Thirty-two patients withdrew from the trial, the most common reasons being adverse events (in 14) and insufficient treatment response (in 8). It is concluded that risperidone is effective, well tolerated, and safe in elderly psychotic patients.

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WIE WIRD RISPERIDON IN DER TÄGLICHEN ANWENDUNG DOSIERT: ZWISCHENERGEBNISSE EINER DEUTSCHEN PHASE IV PRÜFUNG

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Zur Zeit wird in Deutschland eine Phase IV Prüfung durchgeführt mit dem Ziel, die Langzeitanwendung von Risperidon bei der Behandlung der chronischen Schizophrenie unter Alltagsbedingungen zu untersuchen. Die Patienten werden über einen Zeitraum von 2 Jahren beobachtet, in regelmäßigen Abständen werden das Vorhandensein psychotischer Symptome, das psychosoziale Funktionsniveau, die Dosierung und Verträglichkeit evaluiert. Diese Zwischen-auswertung zeigt die Ergebnisse der ersten 886 Patienten, die im ersten Jahr der Studie eingeschlossen wurden über einen Zeitraum von 6 Monaten. Im Mittel waren die Patienten 12 Jahre krank. Die Minussymptomatik war stärker ausgeprägt als die Plussymptomatik. Unter der Behandlung mit Risperidon nahmen sowohl psychotische Symptome als auch vorbestehende extrapyramidalmotorische Symptome sowie die Häufigkeit des Gebrauchs von anticholinerger Medikation ab. Die mittlere Risperidon-Dosis bei Monat 6 war 4.8 ± 1.9 mg pro Tag. Patienten, die mit Neuroleptika vorbehandelt waren, erhielten höhere Risperidon-Dosen als Patienten ohne vorherige neuroleptische Medikation. Im Lauf der Behandlung reduzierte sich die Ko-Medikation mit hochpotenten Neuroleptika, während der Gebrauch von niedrig- und mittelpotenten Neuroleptika als Ko-Medikation im wesentlichen unverändert blieb.

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OVERDOSES WITH 650 MG. OF OLANZAPINE IN A SCHIZOPHRENIC PATIENT

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Olanzapine is an antipsychotic drug that belongs to the tienobenzodiacepine (group) with afinity for the dopaminergic, serotoninergic, adrenergic, histaminergic and muscarinic receptors and a half-life of elimination 30'5 hours. In the present work it's related an intoxication with 650 mg. of Olanzapine (without any other drugs association) in a woman 34 years old, caucasic race, diagnosticated of schizophrenia paranoid with 12 years evolution, she was admitted approximately 8 hours after the ingestion of the drug. Before the arrival of the patient to the Hospital, as related by her relatives, she suffered from a confusional syndrome with language disturbance, ataxia, disorientation, excitement with aggresive behaviour and visual hallucinations. The patient was admitted in the I.U.C. with a coma grade IV/V, intermedium pupils with minimal reaction, hyperreflexia, Babinsky (+), temperature 37'8ºC; tachycardia 180 p.p.m. that required treatment with amiodarone; hypotension (80/50) that needed continuous perfusion with norepinephrine during the first six hours of her admission; E.C.G. was normal at all moments, having a sinusal rythnm, without prolongation of the QT; electrolytic balance which didn't need appropiate diuretic support. In 12 hours time she presented a metabolic acidosis that required bicarbonate perfusion; the agitation episodes decreased with clorazepate 130 mg/day i.v.. After 24 hours she was hemodinamically stable, leaving I.U.C. after 48 hours. During her stay at the Acute Care Unit of Psychiatry neither hematologic and biochemical alterated parameters were present, nor persistent somatic (evaluated by U.K.U.) or cognoscitive (Benton visual retention test and Weschler Adult Intelligence Scale) damages related to the intoxication with Olanzapine.

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TREATMENT OF THE SYMPTOMS OF SCHIZOPHRENIA: A META-ANALYSIS COMPARING RISPERIDONE WITH OTHER ANTIPSYCHOTICS

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Combined data on efficacy were available from 12 double-blind short-term comparative trials of risperidone and other antipsy-

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chotics in patients with chronic schizophrenia. Patients received risperidone (n = 1056; all patients from flexible-dose studies and patients receiving 4–8 mg/day from fixed dose studies), haloperidol (n = 473), or other antipsychotics (n = 703; e.g., haloperidol, levomepromazine, perphenazine, remoxipride, thioridazine, and zuclopenthixol).

At endpoint, the mean decrease from baseline in Positive and Negative Symptom Scale (PANSS) total scores was significantly greater for patients receiving risperidone (−20.9) than haloperidol (−14.3; $p < 0.01$) or other antipsychotics (−16.2; $p < 0.001$). Risperidone-treated patients also showed a significantly greater decrease in the positive ($p < 0.01$), negative ($p < 0.05$), and general psychopathology ($p < 0.001$) subscale scores than patients receiving haloperidol or other antipsychotics. Cluster scores for cognition, affective symptoms, anxiety, and hostility each improved significantly ($p < 0.05$) more for patients receiving risperidone than haloperidol or other antipsychotics.

Efficacy data on patients with an acute exacerbation were available from 7 trials in which patients received risperidone (n = 372), haloperidol (n = 120), or other antipsychotics (n = 285). At endpoint, the mean decrease from baseline in PANSS total scores was significantly greater for patients receiving risperidone (−24.7) than haloperidol (−19.8; $p < 0.05$) or other antipsychotics (−19.8; $p < 0.01$). Risperidone-treated patients also showed a greater decrease in positive symptom scores (−7.8) than those receiving haloperidol (−7.1; $p < 0.1$) or other antipsychotics (−6.3; $p < 0.01$).

These findings are consistent with Phase III trial results that show risperidone is more efficacious than haloperidol for controlling a broad spectrum of symptoms in schizophrenia.

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'SEROQUEL'®: EFFICACY IN IMPROVING MOOD, AGGRESSION AND HOSTILITY OF SCHIZOPHRENIA

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'Seroquel'® (quetiapine), an atypical antipsychotic, has been demonstrated in a clinical trial programme to be effective in the treatment of schizophrenia with no greater EPS than placebo across the full dose range of 150 mg–750 mg/day.

In clinical practice the treatment of depression, aggression and hostility pose particular challenges in management and these problems contribute to increased morbidity and impairment in quality of life.

We present an evaluation of quetiapine in treating the depressive, aggressive and hostile symptoms occurring in schizophrenia using data from four randomised controlled clinical trials. Symptoms were rated using Brief Psychiatric Rating Scale (BPRS) and Clinical Global Impression (CGI). A meta- analysis comparing quetiapine and placebo in treating affective symptoms was carried out on grouped change from baseline, using BPRS factor 1 score, a BPRS mood cluster, the BPRS depression cluster and the BPRS depression item. This analysis demonstrated that quetiapine was associated with a greater proportion of patients showing improvements in affective symptoms and fewer getting worse than with placebo.

Aggression and hostility were measured using BPRS Factor V score, BPRS hostility item and BPRS hostility cluster. In a multiple dose study, in which 5 quetiapine doses (75, 150, 300, 600, 750 mg/day) were compared with placebo and haloperidol (12 mg/day), beneficial effects on the measures of hostility and aggression were evident in the quetiapine groups but not the haloperidol group, reaching significance ($p \leq 0.05$) compared with placebo at doses of 150 mg, 300 mg and 600 mg/day.

These results provide initial evidence, that, in addition to being an effective antipsychotic, quetiapine may have a beneficial effect on low mood, aggression and hostility. This, combined with a favourable EPS and tolerability profile across the dose range, suggests that quetiapine will present a valuable first-line treatment for schizophrenia and other psychotic disorders and may offer an improved quality of life for schizophrenic patients.

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'SEROQUEL'®: A NEW OPTION FOR THE TREATMENT OF SCHIZOPHRENIA WITH NO GREATER EPS THAN PLACEBO

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EPS, especially akathisia, are distressing consequences of standard antipsychotic therapy, often leading to patient dissatisfaction and non-compliance. Therefore, confidence that increasing the dose of an antipsychotic will not lead to greater incidence of EPS is important. A clinical trial programme has demonstrated that 'Seroquel' (quetiapine), over a dose range of 150–750 mg/day, is an effective antipsychotic. Moreover, higher doses of quetiapine were associated with no more EPS than placebo.

We present are EPS data from 4 double-blind, placebo-controlled Phase II/III trials (quetiapine n = 510, placebo n = 206). The proportion of patients reporting EPS adverse events was no different with quetiapine [Q] (7%) than with placebo [P] (12%) and no statistical difference was seen in the proportion of withdrawals due to EPS (Q = 0.2%, P = 0.5%) or proportions of patients receiving anticholinergic medication (Q = 9%, P = 13%). A meta-analysis confirmed these results, demonstrating that there was no difference between quetiapine or placebo in the proportions of patients either showing an improvement (46% and 48% respectively) or worsening (15% and 16% respectively) of EPS as measured by the SAS. Similar results were seen in analyses of AIMS and Barnes Akathisia Scales. This favourable EPS profile has been confirmed in haloperidol-controlled trials in which quetiapine showed superiority over haloperidol irrespective of how EPS was assessed. Furthermore quetiapine showed good general tolerability with a similar withdrawal rate due to adverse events as placebo. There were no statistically significant differences in the proportions of patients on quetiapine and placebo developing clinically significant haematological changes or in effects on plasma prolactin. Quetiapine has good general cardiovascular tolerability: the incidence of clinically significant QTc interval (>500 msec) was lower with quetiapine (0.5%) than with placebo (1.3%).

These data provide reassurance for the clinician that, unlike some other new antipsychotics, the occurrence of EPS, across the full quetiapine dose range, is no greater than that seen with placebo and suggests that 'Seroquel' may be accompanied by a greater degree of patient acceptability.

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EFFECT OF A LOW DOSAGE REGIMEN AMISULPRIDE (50 MG/D) ON EEG, PSYCHOMOTOR AND COGNITIVE PERFORMANCE OF SLEEP-DEPRIVED, HEALTHY SUBJECTS

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Amisulpride (Ami), a substituted benzamide, binds selectively to the dopamine (DA) D_2- and D_3-receptors. It has higher affinity for

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