executive functioning indicate that the RAPP patients display neurocognitive deficits that are comparable to those characterizing adolescents at genetic risk.

The potential of intervention during the prodrome to prevent schizophrenia is a complex and often controversial issue. Ratings obtained from clinicians indicate that the majority of adolescents treated with atypical anti-psychotics (either Olanzapine or Risperidone) in the RAPP clinic have either been stabilized or have shown substantial improvement. The question of whether such clinical benefits are sufficient to outweigh side effects, stigma and the high rate of false positives will also be discussed.

98. A SELF-REPORT QUESTIONNAIRE TO SCREEN FOR PRODROMAL SCHIZOPHRENIA

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The RAPP (Recognition and Prevention of Psychological Problems) Clinic, opened two years ago at Hillside and Schneider Children’s Hospitals (Barbara Cornblatt, Director), is dedicated to the identification, characterization, and treatment of adolescents and young adults with prodromal symptoms of schizophrenia. One major goal of the RAPP Clinic is to develop a brief assessment that will screen for teenagers reporting symptoms thought to characterize the schizophrenia prodrome. As the first step, a self-report instrument including items drawn from the International Personality Disorders Examination Screen (IPDE), a true/false questionnaire that measures each of the ten DSM-IV personality disorders, was routinely administered to all adolescents undergoing intake in Schneider’s outpatient department. Data were collected from two groups of patients: (a) 33 patients later enrolled (blind to IPDE scores) in the RAPP clinic, identified as prodromal based on other clinical information; and (b) 60 patients with other mental disorders (OMD). RAPP patients endorsed significantly more symptoms than OMD patients for odd cluster personality disorders (schizotypal p < .01; paranoid and schizoid, p < .05) and for avoidant personality disorder (p < .05). The RAPP patients did not differ from OMD on any other subscales, indicating specificity of symptom profile. Additionally, a novel index of social isolation was constructed from seven IPDE items; RAPP patients had significantly higher scores than the OMD patients (p = .001). These preliminary findings suggest that a brief self-report assessment has considerable potential for prodromal screening.

99. SAFETY AND EFFECTIVENESS OF OLANZAPINE VERSUS OTHER ANTIPSYCHOTIC DRUGS IN THE TREATMENT OF OUTPATIENTS WITH SCHIZOPHRENIA

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Prospective, comparative, non-randomized, open, observational study, including 2949 outpatients with schizophrenia who were followed up for 6 months after receiving a new prescription of an antipsychotic. Safety was evaluated collecting adverse events and global clinical status was measured through CGI and GAF Scales. A total of 2128 patients received olanzapine, as monotherapy or in combination (Olanzapine group), and 821 received other antipsychotics (Control group). There were no statistical differences between treatment groups at baseline regarding age, gender, disease duration, severity of symptoms, and EPS. Incidence of adverse events and specifically extrapyramidal symptoms was significantly lower in the olanzapine group compared to the control group (p < 0.001). Mean change in the CGI and the GAF was significantly higher in the olanzapine group compared to the control group (p < 0.001). Despite the limitations of an observational study, these results shows that olanzapine is safe and effective in non-selected schizophrenic outpatients, and are consistent with results of previous controlled trials.

100. COMPARATIVE EFFICACY OF OLANZAPINE AND HALOPERIDOL FOR PATIENTS WITH TREATMENT-RESISTANT SCHIZOPHRENIA

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There is relatively little information regarding the efficacy of newer atypical antipsychotic drugs for patients with schizophrenia who are treatment-resistant to neuroleptic agents. Several lines of evidence suggest that a clinical trial of olanzapine in this population is warranted. A sub-population of patients (N = 526) meeting treatment-resistant criteria selected from a large, prospective, double-blind, six-week study assessing the efficacy and safety of olanzapine and haloperidol was examined. Both last-observation-carried-forward (LOCF) and completers (observed cases) analyses were conducted. Olanzapine demonstrated significantly greater mean improvement from baseline in Positive and Negative Syndrome Scale (PANSS) negative symptoms, co-morbid depressive symptoms assessed by the Montgomery-Asberg Depression Rating Scale, akathisia as measured by Barnes Akathisia Scale and extrapyramidal symptoms as measured by Simpson-Angus Extrapyramidal Rating Scale with both LOCF and completers analyses. In addition, olanzapine was significantly superior to haloperidol for Brief Psychiatric Rating Scale (BPRS) total (p = .006), PANSS total (p = .005), and PANSS positive symptoms (p = .017) in completers of the six-week study. Significantly greater response rates were observed in olanzapine-treated (47%) than haloperidol-treated (35%) patients in the LOCF analysis (p = .008), but significance was not reached in the completers analysis (p = .093). Mean doses (±SD) of olanzapine and haloperidol were 11.1 ± 3.4 mg/day and 10.0 ± 3.6 mg/day, respectively. Olanza-
pine was superior to haloperidol for key symptom domains and parkin-
sonian adverse events. Implications of these data for the therapeutics of
this severely ill subgroup are discussed.

101. RELAPSE PREVENTION WITH
OLANZAPINE

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The objective of this study was to assess the efficacy of olanzapine,
compared with placebo in preventing psychotic relapse in stable, mini-
mally symptomatic patients with schizophrenia.

Patients who had been outpatients, minimally symptomatic, and stable
for at least 6 weeks underwent prospective conversion to olanzapine over
the course of 6 weeks followed by an 8-week observation period to
prospectively confirm stability. Patients who were stable on a fixed dose
of olanzapine monotherapy prior to enrollment entered the 8-week
observation phase to confirm stabilization. Following 6 to 14 weeks of
observation, 224 patients were randomized to continued oral olanzapine,
10–20 mg/day and 102 patients were randomized to placebo. Patients
were examined in person at least every 2 weeks and telephone contact
was required if patients were not examined in person at least weekly.
Statistical methods allowing sequential monitoring of relapse rates were
employed to protect against continuing an ineffective treatment.

Based on robust superiority of olanzapine, the study was terminated
early. By Kaplan-Meier analysis, the 6-month cumulative relapse rate for
olanzapine was 6% and for placebo was 55%. The difference between
treatment groups in the time to relapse curves was significant (p <
0.001). Additional efficacy and safety results will be discussed along
with the monitoring techniques.

102. KINETICS AND SAFETY OF A NOVEL
RISPERIDONE DEPOT FORMULATION

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The bioavailability of a new intramuscular depot formulation and of oral
doses of risperidone was assessed in patients with schizophrenia. Three
groups of stable patients with schizophrenia received oral doses of risperi-
done (2, 4, or 6 mg/day) during weeks 1–3 and oral risperidone at half those
doses during weeks 4–5. During weeks 2–10, the three groups received
depot doses of risperidone (25, 50, or 75 mg, respectively) every 2 weeks (5
injections). Plasma concentrations of unchanged risperidone and of the
active moiety (risperidone + 9-hydroxyrisperidone) were determined: Effi-
cacy, adverse events, vital signs, and the injection site were evaluated
regularly. Total daily exposure to the active moiety was equivalent after oral
and depot dosing, i.e., the 90% confidence intervals for the mean steady state
AUC and Cav ratio (depot vs. oral) were all within the bioequivalence range
of 80% to 120%. Peak plasma concentrations were significantly lower (25%
to 32%) after depot than oral dosing. The most frequent adverse events were
either influenza-like symptoms or of a psychiatric nature. No consistent,
clinically relevant changes in vital signs, ECG, or laboratory test results were
observed. Only minor discomfort at the injection site was noted in a few
patients. Patients remained symptomatically stable when treatment was
changed from an oral to a depot regimen. Bioequivalence of oral and IM
depot dosing of risperidone was demonstrated. Moreover, IM depot dosing
was as well tolerated and efficacious as oral dosing.

103. THE IMPLICATIONS OF
ANTIPSYCHOTIC TREATMENT PATTERNS
ON HEALTH OUTCOMES IN
SCHIZOPHRENIA

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We assessed the impact of continuous therapy (CT), intermittent therapy
(IT), or low-exposure therapy (LT) on quality of life in the usual care setting
for patients with schizophrenia. Data on prescribed and dispensed medica-
tions, assessments of quality of life, symptoms, and hospitalizations from a
one-year, naturalistic, randomized clinical trial were analyzed. Of 546
patients who completed the study, 159 were treated with CT (≥90% of study
days on drug), 248 with IT (<90% of days on drug, and intermittent
use), and 139 with LT (≤50% days on drug). Patients were further classified
as receiving monotherapy or polytherapy. SF-36 Mental Component Scores
(MCS) and risk of relapse were compared for each group using regression
models. Relative to LT, patients treated with CT or IT had better MCS at one
year (both p ≤ 0.01). Risk of relapse was lower for patients receiving CT
(OR = 0.33, p < 0.01) and IT (OR = 0.78, p = 0.43), relative to LT. There
were no differences in MCS for patients treated with monotherapy or
polytherapy, however, patients receiving monotherapy had a 69% lower risk
of relapse (p < 0.01). These results suggest a high proportion of patients in
usual care do not receive optimal maintenance therapy following acute
relapse. Continuous therapy was associated with better quality of life and
relapse prevention than other patterns of treatment, and monotherapy
reduced patients’ risk of relapse.

104. RISPERIDONE VS HALOPERIDOL FOR
RELAPSE PREVENTION IN
SCHIZOPHRENIA AND SCHIZOAFFECTIVE
DISORDER: A LONG-TERM DOUBLE-
BLIND COMPARISON

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A multicenter, randomized, double-blind comparison of risperidone
(RIS) and haloperidol (HAL) in stable outpatient schizophrenics and
patients with schizoaffective disorder was conducted to compare the time
to relapse. Patients continued double-blind treatment until the last patient
had completed 1 year. Assessments were made weekly for the first 4
weeks and at 4-week intervals thereafter. Scales used to assess efficacy
included the total score on PANSS and all PANSS subscale scores.
Safety evaluations included ERS and clinical laboratory tests, including
weight gain. Of 365 treated patients in the trial, 41 (23.2%) in the RIS
and 65 (34.6%) in the HAL groups relapsed by the end of the first year
(P = .009). During the entire trial, 45 (25.4%) patients on RIS and 75
(39.9%) patients on HAL relapsed (P = .002). Patients in the RIS
group experienced only a modest degree of weight gain (5.0 lbs at
endpoint), a low rate of TD (0.6%), and a low rate of EPS. This study
provides evidence for the long-term effectiveness of RIS and corrobora-
tes earlier pivotal trials in which RIS was found to be significantly