Introduction

A number of studies have demonstrated that atypical antipsychotics, such as quetiapine (Seroquel®), risperidone and olanzapine, have superior efficacy compared with conventional agents, in particular for negative, affective and cognitive symptoms.1 In addition, atypical antipsychotics are less likely to cause extrapyramidal symptoms (EPS).2

Quetiapine and risperidone have been compared directly in two clinical studies3,4 with the results demonstrating that quetiapine was at least as effective as risperidone but was better tolerated, particularly with regard to EPS and plasma prolactin changes.

Comparative clinical studies comparing olanzapine and risperidone demonstrated similar efficacy; however, olanzapine-treated patients gained weight compared with risperidone-treated patients.5

Although a recent meta-analysis has demonstrated that quetiapine, risperidone and olanzapine have similar efficacy,6 no study has directly compared the efficacy, safety and tolerability of these three atypical antipsychotics.

Objectives

The aim of the present study is to directly compare the efficacy, safety and tolerability of quetiapine with olanzapine and risperidone in patients with schizophrenia. The interim results after 8 weeks of treatment are reported in this paper.

Methods

Study Design

A randomised, rater-blinded, flexible-dose study is being conducted over 16 weeks. Patients randomised to quetiapine 600 mg/day, olanzapine 15 mg/day and risperidone 5 mg/day. The following were assessed at each weekly clinic visit

- PANSS total score
- PANSS negative and positive subscale scores
- Brief Psychiatric Rating Scale (BPRS) Factor V
- change from baseline in BPRS hostility cluster scores

The following were assessed at each weekly clinic visit

- Simpson-Angus Scale (SAS)
- Barnes Akathisia Rating Scale (BARS)
- Change from baseline in EPS, as measured by the SAS at Week 8.

Efficacy assessment

The following were assessed at each weekly clinic visit

- PANSS total score and negative and positive subscale scores
- Brief Psychiatric Rating Scale (BPRS) Factor V
- change from baseline in BPRS hostility cluster scores
- PANSS negative subscale score at Week 8 (%)

Tolerability assessments

- At each weekly clinic visit, EPS were assessed using the Simpson-Angus Scale (SAS) and Barnes Akathisia Rating Scale (BARS)
- Vital signs and body weight were also recorded.

Statistical analysis

- At this interim stage in the study, no analysis of statistical significance has been performed.
- All mean scores have been calculated on a last observation carried forward (LOCF) basis.

Results

Patients and treatment

- A total of 120 patients have been recruited to date: 20 patients have been randomised to quetiapine, 10 to olanzapine and 10 to risperidone.
- The mean age of patients was 46.7, 32.0 and 44.4 years for the quetiapine, olanzapine and risperidone groups, respectively.
- Overall, the majority of patients were male 42.0%, 73.0% and 50.0% for quetiapine, olanzapine and risperidone, respectively.
- During the first 6 weeks, the mean doses administered were quetiapine 840 mg/day, olanzapine 15 mg/day and risperidone 5 mg/day.

At Week 8, 36% of patients treated with olanzapine had a weight gain of ≥5% from baseline, while 17% and 13% of patients treated with risperidone and quetiapine, respectively, fell into this category.

Conclusions

This study is the first to directly compare three atypical antipsychotic agents (quetiapine, olanzapine and risperidone). These data suggest that the three atypical antipsychotics have similar efficacy over the 8 week period; with all three drugs improving positive and negative symptoms to a similar degree. However, there are significant differences in their tolerability profiles.

- Treatment-emergent EPS (including akathisia) occur more often with risperidone than with quetiapine and olanzapine. Risperidone patients had developed clinically significant symptoms of akathisia by Week 6, while a higher incidence of weight gain was seen with olanzapine compared with the other two agents.

In conclusion, the interim results suggest that quetiapine is as effective as risperidone and superior to olanzapine, in terms of a more favourable tolerability profile. The final results of the study are awaited with interest.