Background

It is not known whether switching antipsychotics or early use of clozapine improves outcome in (first-episode) schizophrenia.

Methods

The study was conducted in 27 centres in 14 European countries and Israel consisting of general hospitals and psychiatric specialty clinics. (Clinicaltrials.gov identifier is NCT01248195). Patients with schizophrenia or schizophreniform disorder were treated for four weeks with up to 800 mg/day amisulpride in an open design. Patients who did not meet symptomatic remission criteria at four weeks were randomized to continue amisulpride or switch to olanzapine (max 20 mg/day) during a six-week double blind phase. Patients who were not in remission at ten weeks were given clozapine (max 900 mg/day) for an additional 12 weeks in an open design. Data were analyzed using a generalised linear mixed model, with a logistic link and binomial error distribution.

Findings

Participants were recruited between May 26, 2011 and May 15, 2016 with 481 signing informed consent. Of the 446 patients in the ITT sample, 371 (83.2%) completed open amisulpride treatment, of whom 250 (67.4%) were in remission. 93 of the patients who were not in remission continued to the six-week double-blind switching trial with 72 patients (77.4%) completing it (39 on olanzapine and 33 on amisulpride); 15 (45.5%) of the patients taking amisulpride reached remission versus 17 (43.6%) on olanzapine (p=.87). Of the 40 patients who were not in remission after 10 weeks of treatment, 28 (70.0%) were started on clozapine; 18 patients (64.3%) completed the 12-week treatment, of whom five (27.8%) met remission criteria.

Conclusions

In the large majority of patients in the early stages of schizophrenia, symptomatic remission can be achieved using a simple treatment algorithm comprising the sequential administration of amisulpride and clozapine.