Post-hoc analysis of drop-out in 2 clinical trials of customized adherence enhancement + long-acting injectable antipsychotic for high-risk individuals with schizophrenia

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Methodological Question Being Addressed: What are factors that may minimize drop-out in a clinical intervention trial in high-risk schizophrenia?

Aims: Long-acting injectable antipsychotic medication (LAI) can be a practical treatment option to optimize adherence for high-risk groups such as homeless individuals with serious mental illness (SMI). These investigators have developed a Customized Adherence Enhancement (CAE) approach that improves outcomes when added to LAI for homeless or recently homeless individuals with schizophrenia or schizoaffective disorder. For this analysis, data from 2 prospective, 6-month open-label, uncontrolled studies involving individuals with schizophrenia/schizoaffective disorder were pooled. Study design was nearly identical except that LAI used was haloperidol decanoate in study 1 and paliperidone palmitate in study 2. The CAE approach in study 2 was delivered by a licensed social worker and enhanced by more extensive outreach to community mental health clinics. This analysis investigated drop-out patterns, which are a significant problem in schizophrenia clinical trials.

Methods: Both trials combined CAE + LAI in 30 recently homeless individuals with schizophrenia or schizoaffective disorder for a total combined sample of 60. Clinical outcomes included medication adherence using the Tablets Routine Questionnaire (TRQ), LAI injection frequency and psychiatric symptoms measured by the Positive and Negative Syndrome Scale (PANSS), Brief Psychiatric Rating Scale (BPRS) and global psychopathology (Clinical Global Impressions /CGI). Social functioning was assessed via the Social and Occupational Functioning Assessment Scale (SOFAS).

Results: Mean combined age of the sample was 42.7 years (SD=9.0), mainly minorities (88.3% African-American), mainly single/never married (71.2%) with a mean of 11.4 years of education. Baseline rate of substance abuse within the past year was 25.0%, and rate of incarceration within the past 6 months was 21.6 %. A total of 14 individuals (23.3 %) terminated the study prematurely (prior to the 6-month endpoint). Demographic and clinical features did not predict drop out. Drop-out rate in study 1 (33.3%) trended higher compared to study 2 (13.3%) (p=.08). For both studies, most drop-outs occurred in the early portion of the clinical trial (mean of 58.8 (SD =36.0) and 56.0 days (SD = 42.0), respectively). Completers had significant improvement in adherence, psychiatric symptoms, global psychopathology and functioning.

Conclusion: Highly symptomatic SMI is common in the homeless population and LAI combined with a targeted adherence enhancement approach may be a useful therapeutic approach in these high-risk individuals. Using an LAI that minimizes extrapyramidal burden and including social workers who are trained to interface with community mental health clinic staff in typical treatment settings may minimize trial drop-out. Additional intensive efforts may be needed early in the course of treatment, especially during the first 2 months, to help these individuals remain in treatment.