

# A Cluster-Randomized Large, Simple Trial To Compare A Long-Acting Injectable Antipsychotic To Oral Antipsychotics In The Early Course Of Schizophrenia

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## METHODOLOGICAL QUESTION

Patient-randomized RCTs comparing oral and long-acting injectable (LAI) antipsychotics for schizophrenia have often failed to demonstrate advantages for LAIs. Methodological questions raised by these trials include target population (older and possibly more adherent than usual due to agreeing to treatment randomization) and the effects of the added attention and frequency of visits in a RCT.

## INTRODUCTION

The PRELAPSE study addresses these concerns in a cluster-randomized, large simple trial being conducted in the US for patients aged 18 to 35 years with a confirmed SCID-5 diagnosis of schizophrenia and less than five years antipsychotic medication exposure.

## METHODS

### STUDY DESIGN

- Cluster-randomized trial
- 39 sites in 19 US states randomized to offer antipsychotic treatment
- 19 sites randomized to LAI Aripiprazole Once Monthly (AOM)
- 20 sites randomized to Clinician's Choice (CC) of antipsychotic
- Two-year treatment/observation duration for subjects

### SUBJECTS

- SCID-5 confirmed schizophrenia diagnosis
- Age 18-35
- Less than five years of documented antipsychotic medication exposure

### ASSESSMENT STRATEGY

- Designed to minimize effects of trial participation
- Central blinded raters using secure on-line video assessment: Diagnosis at baseline; symptom ratings at baseline, 1 and 2 years  
Site teams: Logs of hospitalization and emergency room visits and adverse event assessment

PRIMARY OUTCOME: Time to first hospitalization

STUDY ENROLLMENT: Between 12/2014 and 12/2016

## RESULTS

As presented in the Table, a total of 672 patients consented to the study and 489 of these met eligibility criteria.

	Consented	Withdrew before completing eligibility assessment	Eligible	Did not meet eligibility criteria
AOM	N=328	N=48	N=234	N=46
Clinician Choice	N=344	N=45	N=255	N=44

The final study sample included 366 men (75%) and 123 women (25%). The mean age was 25.2 (SE=0.2) years. The most common racial backgrounds were African American (N=213, 43.6%) and White (N=171, 35.0%). Forty-eight percent of subjects had 1 year or less of lifetime antipsychotic exposure.

At AOM sites, 212 participants received at least 1 study AOM injection.

## CONCLUSIONS

These data suggest that it is possible to conduct a large simple trial utilizing cluster randomization to assess the potential impact of LAI antipsychotics in reducing rates of hospitalization.

The success of such a study depends on having a very high proportion of eligible patients in the "experimental" sites agreeing to receive injections. We have demonstrated that this goal can be achieved, even in early phase patients.

## ACKNOWLEDGEMENTS

The study is supported by a grant from Otsuka US.

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## DISCLOSURE

Dr. Kane has been a consultant for or has received honoraria from Alkermes, Eli Lilly, EnVivo Pharmaceuticals (Forum), Forest, Genentech, H. Lundbeck, Intracellular Therapeutics, Janssen Pharmaceuticals, Johnson and Johnson, Otsuka, Reviva, Roche, Sunovion, and Teva and is a shareholder in Med-Avante, Inc., LB Pharmaceuticals and Vanguard Research Group. Dr. Schooler has served as consultant or on advisory boards for Alkermes, Allergan, Forum (formerly EnVivo), and Sunovion. Dr. Robinson has been a consultant or received grants from Asubio, Bristol-Myers Squibb, Janssen, Otsuka, and Shire. Dr. Achtyes has received research support from Alkermes, AssurEx, Avanir, Boehringer Ingelheim, Janssen, Neurocrine Biosciences, Novartis, Otsuka, Pfizer, Pine Rest Foundation, Priority Health, Network180 and Vanguard Research Group and served on an advisory panel for Roche, Janssen and the Vanguard Research Group. Ms. Marcy is a shareholder in Pfizer and is the executive director of the Vanguard Research Group, which has received research support from Otsuka, Alkermes, Lundbeck, and Janssen.