






## The GiSAS study: Rationale and design of a pragmatic randomized controlled trial on aripiprazole, olanzapine and haloperidol in the long-term treatment of schizophrenia ☆

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## Abstract

Given the controversy about the comparative efficacy of first- compared with second-generation antipsychotics in the treatment of schizophrenia, more large-scale evidence is needed to guide clinicians in their prescriptions. Most randomized controlled trials (RCTs) were conducted in centers of excellence on highly selected samples, poorly representative of real-world patients, and often suffered conflicts of interest as they were sponsored by drug companies.

The primary aim of the present study is to compare the effectiveness of haloperidol, olanzapine and aripiprazole in a representative sample of schizophrenia patients. The GiSAS trial is an open-label, independent, pragmatic RCT in Italian community-based public psychiatric services. At least 260 patients meeting the DSM-IV criteria for schizophrenia will be randomly allocated to one of the study drugs and followed up for one year. A two-year observational phase will follow. The primary outcome for tolerability will be the onset of metabolic syndrome. The primary endpoint for effectiveness will be discontinuation of antipsychotic monotherapy. Secondary measures include global functioning, time to discontinuation due to side-effects, change of lipid profile, extrapyramidal symptoms and other adverse effects.

In the last four years, the GiSAS study group has been working to implement this multicenter RCT. The trial mechanism is now fully functional and working. As of end of February 2011, 260 subjects were randomized by 54 study investigators in 33 out of 43 participating centers.

## Keywords

- Antipsychotic;
- Schizophrenia;
- Pragmatic trial;
- Metabolic syndrome;
- Drug discontinuation

## Abbreviations

- ATP, Adult Treatment Panel III;
- CATIE, Clinical Antipsychotic Trials of Intervention Effectiveness;
- CUTLASS, Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia;
- EPS, Extrapyramidal symptoms;
- EUFEST, European First Episode Schizophrenia Trial;
- FGAs, First-generation antipsychotics;
- GAF, Global Assessment of Functioning;
- GiSAS, Italian Group for the Study of Second-generation Antipsychotics;
- ITT, Intention to treat;

- LUNRSERS, Liverpool University Neuroleptic Side Effect Rating Scale;
- SGAs, Second-generation antipsychotics

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DRUG DISCONTINUATION MODULE

PLEASE MARK THE MAIN REASON FOR DRUG DISCONTINUATION

DISCONTINUATION date:

0

LACK OF EFFICACY

→

☐ clinician's decision

☐ patient's decision

☐ shared decision

Please specify:

1

POOR TOLERABILITY

→

☐ clinician's decision

☐ patient's decision

☐ shared decision

Please specify:

2

PATIENT'S OWN INITIATIVE

→

☐ clinician's decision

☐ patient's decision

☐ shared decision

Please specify:

3

CLINICAL REMISSION


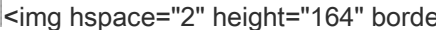

→




☐ clinician's decision



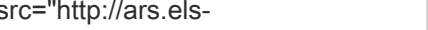
☐ patient's decision




☐ shared decision

Please specify:


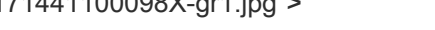

  

Fig. 1. The study drug discontinuation module in the trial monitoring form.

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Table 1. Examples of independently funded pragmatic RCT on long-term effectiveness of antipsychotic therapy in schizophrenia.


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*Trial Registration.* ClinicalTrials.gov Identifier NCT01052389.



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<http://www.gisas.marionegri.it>.

2

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