

# Randomized Olanzapine Clozapine Key study on Schizophrenia and Addiction in the Netherlands (ROCKSAN)

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Primary research questions: 1. Is there a difference in effectiveness of clozapine treatment compared to olanzapine treatment in the reduction of substance use disorders of patients with schizophrenia and related psychotic disorders? 2. What is the...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Pending
<b>Health condition type</b>	Other condition
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON32733

### Source

ToetsingOnline

### Brief title

ROCKSAN

### Condition

- Other condition
- Schizophrenia and other psychotic disorders
- Lifestyle issues

### Synonym

addiction, psychosis, schizophrenia, substance abuse

### Health condition

verslaving

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum

**Source(s) of monetary or material Support:** ZonMW

## Intervention

**Keyword:** clozapine, olanzapine, randomized, schizophrenia, substance abuse

## Outcome measures

### Primary outcome

1. At baseline, week 4, week 8, month 6 or at moment of withdrawal from the study: Self reported substance use - CIDI section B,J,L and Recent Drug Use

Urinalysis

2. Cost-effectiveness - Incremental cost-effectiveness ratio (ICER): difference in costs/the difference in effectiveness (clozapine-olanzapine).

### Secondary outcome

1. Direct and indirect medical costs, and non-medical costs

2. Other clinical outcome: - Psychopathology: PANSS, YBOCS, OCDUS, QoL, SWN, CGI, GAF, LCS,

- Adverse effects: - leucopenia, agranulocytosis, - Time to non- compliance, -

Time to withdrawal from study, - Quality of life, Quality adjusted life years (QALYs)

## Study description

### Background summary

The lifetime prevalence of substance use disorders (SUD) of patients with

schizophrenia is about 50%. Substances commonly abused by patients with schizophrenia include nicotine, alcohol, cannabis, cocaine and amphetamines. Co-morbid substance abuse is associated with poor outcome. There are some indications that clozapine has a favourable effect on SUD in schizophrenia. These possible benefits should be weighed against the risk of adverse effects. If this study proves that clozapine is effective in reducing SUD of patients with schizophrenia, clozapine should get a more prominent place in the treatment protocol of patients with SUD and schizophrenia.

## **Study objective**

Primary research questions: 1. Is there a difference in effectiveness of clozapine treatment compared to olanzapine treatment in the reduction of substance use disorders of patients with schizophrenia and related psychotic disorders? 2. What is the Incremental cost-effectiveness ratio (ICER): the difference in costs / difference in effectiveness of clozapine treatment compared to olanzapine treatment?

Secondary research questions: 1. Are there differences in direct and indirect medical costs and non-medical costs between clozapine treatment and olanzapine treatment? 2. Are there differences in effectiveness of clozapine treatment compared to olanzapine treatment in: psychopathology, adverse effects, compliance, drop out rate, psychosocial functioning and quality of life?

## **Study design**

A 6 month multi-centre randomized, double blind study

## **Intervention**

clozapine flexible dose 200-600 mg, olanzapine flexible dose 10 mg-30 mg

## **Study burden and risks**

Burden: Patients will be randomly allocated to receive clozapine or olanzapine. One extra session is needed to inform patients on the study design and procedure. Four extra sessions are needed to assess baseline and outcome data.

Risk: There is a risk on adverse effects related to the treatment with clozapine or olanzapine. Careful clinical procedures will be performed to detect adverse effects and respond to them as needed. To keep the blinding it is necessary to perform the same routine blood monitoring in both treatment groups. Some extra blood samples will be taken for future research on proteins, which may function as biological marker for treatment. Benefit: study medication may be associated with favourable effects.

## Contacts

### Public

Academisch Medisch Centrum

Meibergdreef 5  
1105 AZ Amsterdam  
NL

### Scientific

Academisch Medisch Centrum

Meibergdreef 5  
1105 AZ Amsterdam  
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

Eligible for the study are in- and outpatients age 18 to 50, meeting DSM-IV criteria for schizophrenia, schizoaffective - or schizophreniform disorder and substance abuse or dependence based on the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (SCID-P).

Patients that are admitted under authority of the court should also be included, since this group embodies a very large percentage of the targetgroup.

Patients should be able to understand the study information and procedures and give informed consent.

## Exclusion criteria

- Pregnancy
- Lactating women
- Female subject without adequate contraception
- Known hypersensitivity to clozapine, olanzapine or ingredients used in these tablets
- Concomitant daily use of any antipsychotic other drug than clozapine or olanzapine (crisis intervention medication excepted)
- Use of depot antipsychotics in the three months prior to inclusion
- Narrow-angle glaucoma
- Known neurological or endocrine disease interfering with clozapine or olanzapine treatment
- Myeloproliferative disorder
- Uncontrolled epilepsy
- History of treatment with clozapine in the past 12 months during at least 4 months at therapeutic serum levels
- Paralytic ileus
- Current leukocyte level lower than  $3.5 \times 10^9/l$
- Current neutrophilic granulocyte level lower than  $2.0 \times 10^9/l$

## Study design

### Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

### Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-10-2008
Enrollment:	140
Type:	Anticipated

## Medical products/devices used

Product type:	Medicine
Brand name:	Clozaril
Generic name:	Clozapine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zyprexa
Generic name:	Olanzapine
Registration:	Yes - NL intended use

## Ethics review

Approved WMO	
Date:	22-12-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

Register	ID
EudraCT	EUCTR2008-005019-16-NL
CCMO	NL24882.018.08