Raloxifene augmentation in patients with a schizophrenia spectrum disorder to reduce symptoms and improve cognition

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON55630

Source
ToetsingOnline

Brief title
Raloxifene Augmentation in Patients with a Schizophrenia spectrum Disorder

Condition

- Schizophrenia and other psychotic disorders

Synonym
schizoaffective disorder, schizophrenia

Research involving
Human

Sponsors and support

Primary sponsor: Psychiatrie
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: cognition, raloxifene, schizophrenia, selective estrogen receptor modulator

Outcome measures

Primary outcome

The primary objective of this trial is to investigate the beneficial effect of raloxifene as compared to placebo when given for twelve weeks in addition to antipsychotic medication. We expect to find lower severity of psychotic and cognitive symptoms as measured with the Positive And Negative Symptom Scale (PANSS) and the Brief Assessment of Cognition in Schizophrenia (BACS) over the course of 12 weeks.

Secondary outcome

Secondary outcomes are changes in negative symptoms (measured with BNSS), changes in personal and social performance (measured with PSP), change in severity of thought disorder (measured with TALD), quality of life (measured with EQ-5D), use of healthcare and non-healthcare resources, comorbid depression (measured with BDI), cognitive control (measured with a Stroop Test), language production (measured by analyzing speech samples), DNA-profiles and hormonal and inflammatory biomarkers.

Study description

Background summary

There is ample evidence that sex hormones may influence the course of schizophrenia. Women with schizophrenia have a greater likelihood of developing psychosis when estrogen levels are low, for instance around menopause. Several trials have evaluated estrogen augmentation in women with schizophrenia,

however, long-term treatment is not safe as it has considerable side effects. Selective Estrogen Receptor Modulators (SERMs), such as raloxifene, do not carry these side effects. Three trials have described positive effects of raloxifene augmentation in postmenopausal women with schizophrenia. To this date, only one trial has studied the addition of raloxifene in premenopausal women and in men, which show significant improvement on cognition but not on psychotic symptoms. Their findings confirm the potential of raloxifene for general use in patients with schizophrenia. At least one independent replication is needed to guarantee implementation into clinical practice. Furthermore, if a correlation between baseline hormonal levels and raloxifene efficacy can be observed, this study can be used to start personalized psychiatry.

Hypotheses: Daily treatment with raloxifene 120mg in addition to antipsychotic treatment increases social and personal functioning, improves cognition, reduces psychotic symptoms and health care costs, as compared to placebo.

Study objective

The primary objective of this trial is to investigate the proposed beneficial effect of raloxifene as compared to placebo when given for twelve weeks in addition to antipsychotic medication to patients with a psychotic disorder. We expect lower severity of psychotic and cognitive symptoms as measured with the Positive And Negative Symptom Scale (PANSS) and the Brief Assessment of Cognition in Schizophrenia (BACS).

Secondary objectives concern change in negative symptoms as measured with the Brief Negative Symptom Scale (BNSS) in functional outcome (PSP), change in severity of thought disorder (TALD), change in health-related quality of life and quality adjusted life years (QALY) outcomes using the EQ-5D, change in cognitive control (Stroop Test), change in use of healthcare and non-healthcare resources (using the institute for Medical Technology Assessment*s Medical Consumption Questionnaire (iMTA-MCQ) and Productivity Cost Questionnaire (iMTA-PCQ) respectively), change in comorbid depression will be monitored using Beck*s Depression Inventory (BDI) and change in productive language will be tested by analyzing speech recordings.

Study design

Randomized placebo-controlled multicenter double-blind trial

Intervention

Patients will be randomized 1:1 to either 120mg raloxifene or placebo daily, in the form of identical tablets.

Study burden and risks

Use of raloxifene is associated with a small risk of side effects. The number of patient visits will be limited to 4 visits and mainly requires time invested for physical examinations, questionnaires and cognitive testing sessions (around 9 hours in total over the course of 9 months). Blood will be drawn at three occasions with negligible and known risks (e.g. irritation). The burden and risks are acceptable while the benefits are expected to be considerable.

Contacts

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Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- A DSM-IV-R diagnosis of: 295.x (schizophrenia, schizophreniform disorder,

schizoaffective disorder, or psychotic disorder NOS)
- Capable of understanding the purpose and details of the study in order to provide written informed consent;
- Use of antipsychotic medication and being on a stable dose of antipsychotic medication for at least two weeks;
- Age over 18 years.,
For female patients:
- Female patients of childbearing potential (WOCBP; i.e. fertile, following menarche and until becoming post-menopausal unless permanently sterile after hysterectomy, bilateral salpingectomy and bilateral oophorectomy) who are sexually active must be willing and capable to use a non-estrogenic contraceptive (intrauterine device, cervical cap, condom or diaphragm) in case of sexual intercourse for the complete duration of the study;
- Female patients with post coital uterine bleeding must have documented normal PAP smear and pelvic examination in the preceding five years. If no documented PAP smear is present, female patients with post coital uterine bleeding must be willing to undergo a PAP smear .
- Female patients between the age of 52 and 75 must have a reported normal mammogram as part of the Dutch *bevolkingsonderzoek* in the preceding two years. In case a patient has not participated in the regular breast cancer screening, female patients between de age of 52 and 75 must be willing to undergo a mammogram.

Exclusion criteria

-Pre-existing cardiovascular disease (not including hypertension);
-History of thrombo-embolic events;
-Familial tendency to form blood clots (such as familial factor V Leiden);
-Use of vitamin K antagonists;
-Use of cholestyramine or other anion exchange resins;
-Hypertriglyceridemia (triglycerides > 3 times the upper limit of normal (ULN));
-History of breast cancer;
-Liver function or enzyme disorders (serum bilirubin, alkaline phosphatase (AF), gamma-glutamyl transpeptidase (* - GT), aspartate aminotransferase (ASAT) or alanine aminotransferase (ALAT) > 3 times the ULN as measured at baseline);
-Severe kidney failure (eGFR <30 ml/min as measured at baseline)
-Use of any form of estrogen or androgen as hormonal therapy, or antiandrogen including tibolone or use of phytoestrogen supplements as powder or tablet in the past three months., For female patients:
- Pregnancy or breast feeding

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2016
Enrollment:	95
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Evista
Generic name:	raloxifene hydrochloride
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-02-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	08-07-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-10-2016

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-12-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-07-2021

Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2015-004483-11-NL
CCMO	NL55343.041.16