Trial Examining Methods for Antidepressant Discontinuation

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON55952

Source
ToetsingOnline

Brief title
TEMPO

Condition

- Mood disorders and disturbances NEC

Synonym
depression, major depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Antidepressants, Discontinuaton, Withdrawal symptoms

Outcome measures

Primary outcome

Rate of failure to successfully discontinue antidepressant: defined as significant deviation from discontinuation antidepressant protocol (e.g. switching to rescue medication (>=5 days in total), stopping with discontinuation medication) or significant withdrawal symptoms (increase in modified 15-item DESS score from baseline >4 for at least two consecutive assessments).

Secondary outcome

We will additionally evaluate i) long-term effects, including relapse/recurrence of an MDD-episode during 38 weeks of follow-up after discontinuation; ii) identify predictors for who is at increased risk for experiencing such a recurrence; iii) investigate cost-effectiveness of the two discontinuation strategies. If patients fail to discontinue their antidepressants during the double-blind phase, a secondary open label follow up is offered to those wanting to continue their attempt to discontinue and participate in a personalized part of the protocol.

Study description

Background summary

Two different ways of antidepressant discontinuation currently exist: 1) a conventional reduction which halves dosages with available dosage-units and

stop over the course of weeks (currently treatment as usual), and 2) a more gradual dose reduction with progressively smaller dosage-units over a longer period. However, it is currently unknown whether one method is preferred about the other, and these two ways of antidepressant discontinuation have not been directly compared in a double-blind RCT. This lack of evidence leaves patients, clinicians, pharmacists and policy-makers uncertain about rational methods to discontinue antidepressants.

Study objective

This study has been transitioned to CTIS with ID 2024-511997-66-00 check the CTIS register for the current data.

TEMPO will directly compare i) conventional 2-step reduction with ii) gradual tapering in patients with remitted MDD who use either the antidepressant paroxetine (PAR) or venlafaxine (VLX). We will evaluate the number of patients that can successfully discontinue PAR or VLX between arms, based on either discontinuation symptoms or relapse of major depressive disorder (MDD).

Study design

Multicenter double-blind randomized (1:1) clinical trial of 200 patients with remitted MDD (assessed with semi-structured interview) using paroxetine (PAR, 20-50mg, n=100) or venlafaxine extended release (VLX, 75-375mg, n=100). The double-blind discontinuation phase is followed by an open label phase without medication, while blinding of tapering-method is maintained. With patients who drop-out during discontinuation, after unblinding, we will discuss an alternative, open label discontinuation plan, chosen via shared decision making, to enable another (prospectively monitored) discontinuation attempt.

Intervention

Concealed stratified block randomization by computer (1:1) to: i) conventional tapering strategy (N=100 [~50 PAR/~50 VLX]) or ii) gradual tapering strategy (N=100 [~50 PAR/~50 VLX]) over a 16-week period.

Study burden and risks

Discontinuation of antidepressants can cause withdrawal symptoms and relapse patterns might be less favorable when antidepressants are discontinued less slowly compared to gradual tapering, which is unknown and a secondary outcome of this study. However, these risks are not higher during this study than those of antidepressant discontinuation in daily clinical practice. Because the clinical population under study is vulnerable for recurrences of depression, we classify the risk as moderate. To decrease the risk of experiencing withdrawal symptoms, we use relatively slow tapering of the antidepressant dose in the

conventional arm, which is also done in current clinical practice and in line with Dutch clinical guidelines and the multidisciplinary document *Afbouwen SSRI*s en SNRI*s'.
The burden of the study for patients consists of making time to visit the study center 6-9 times during a year, have an additional 12-14 telephone assessments and fill out questionnaires regularly from their own home and on their smartphone. Furthermore, it may be confronting for depressed individuals to be asked about their mood and possible suicidal ideation. There will be two blood draws, done by a fieldworker or researcher who is qualified to draw blood thereby minimalizing the risk of injury.
Adverse side effects and withdrawal symptoms, medication adherence, and depressive and suicidal symptoms will be closely monitored with structured measurement instruments. SAEs and SUSARs will be closely monitored as well. There will be close contact between the physicians/pharmacists of the TEMPO research team and the patient*s own physician in case of relapse or severe withdrawal symptoms. Overall we consider the risk of this study as moderate.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

To be eligible to participate in this study, a subject must meet all of the following criteria: • Age 18-75 years • Stable >=6-month (>=1 year in recurrent MDD) remission of MDD, with remission defined as score of <=12 on PHQ-9 questionnaire • Confirmed >6 months use of PAR (20-50mg) or VLX (75-375mg) • Previous MDD episode and current remission confirmed with semi-structured psychiatric interview (MINI). • Willing and able to provide informed consent and follow the procedures necessary to participate in the study

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Psychotic/bipolar disorder
• Severe drug/alcohol addiction that warrants clinical attention
• Insufficient mastery of Dutch language.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-01-2023

Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Paroxetine
Generic name:	Paroxetine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Venlafaxine ER
Generic name:	Venlafaxine ER
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-12-2023
Application type:	Amendment
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

ID: 29528
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EU-CTR	CTIS2024-511997-66-00
EudraCT	EUCTR2021-006108-34-NL
CCMO	NL79723.029.22
Other	NTR: NL9867