Trial Examining Methods for Antidepressant Discontinuation

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Succes-rate of discontinuation is higher with more gradual tapering of paroxetine or venlafaxine

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Depressed mood disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON29528

Source
Nationaal Trial Register

Brief title
TEMPO

Condition

- Depressed mood disorders and disturbances

Synonym
Paroxetine, venlafaxine, discontinuation, tapering, hyperbolic

Health condition

Major Depressive Disorder

Research involving
Human

Sponsors and support

Primary sponsor: AmsterdamUMC

Secondary sponsors:	Radboudumc
Source(s) of monetary or material Support:	ZonMW Goed Geneesmiddelen Gebruik

Intervention

Explanation

Outcome measures

Primary outcome

The number of patients who are unable to successfully continue to taper the PAR or VLX and stop taking study-medication or take rescue medication

Secondary outcome

- Withdrawal symptom severity over time (DESS-score) - Depressive symptoms over time (IDS-SR) - Relapse/recurrence rate (MDD diagnosis on MINI interview) and time to event during follow-up - Daily functioning and Quality of life (EQ-5D-5L) - Attitudes towards and perceived difficulty of discontinuation (patient reported) - Cost-effectiveness and productivity losses (TiC-P) - Before and after discontinuation choice and decision times on a task requiring participants to choose how much effort to exert for various amounts of reward

Study description

Background summary

Rationale: For discontinuation, two fundamentally different ways of antidepressant discontinuation exist: 1) a conventional 2-step reduction, halving dosages with available dosage-units and then stop over 2-4 weeks (currently treatment as usual), and 2) more gradual reduction (dose reduction with progressively smaller dosage-units). The crucial difference between these ways of antidepressant discontinuation are free-fall vs. linear decreases of SERT occu¬pancies, respectively. These two ways 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. Objective: TEMPO will compare two tapering strategies in patients with remitted MDD who use either paroxetine (PAR) or venlafaxine (VLX). We will evaluate effectiveness (number of patients that can discontinue their antidepressant; depression-scores and discontinuation symptoms), pharmacokinetics during the course of discontinuation, relapse rates during 6 months of follow-up after deblinding, patients attitudes and perceived difficulty during discontinuation and cost-effectveness. Study design: Multicenter randomized (1:1) clinical trial of 200 patients with remitted major depressive disorder (MDD, retrospectively assessed

by semi-structured interview) using paroxetine (PAR, 20-50mg, n=100) or venlafaxine (VLX, 75-375mg, n=100). After double blind discontinuation of antidepressants, we will follow patients up for ≥6 months (no medication or blindng). Study population: Patients (18-75 years) with stable 6-month remission of MDD with confirmed >6 months use of PAR (20-50mg, N=100) or VLX (75-375mg, N=100). Exclusion criteria are psychotic/bipolar disorder, severe drug/alcohol addiction, insufficient mastery of Dutch language. Intervention: Concealed randomization by computer (1:1) to either of the two tapering strategies. Main study parameters/endpoints: Rate of failure to successfully discontinue antidepressant: defined as significant deviation from discontinuation antidepressant protocol (e.g. switching to rescue medication, stopping with discontinuation medication) or significant withdrawal symptoms during the double blind phase.

Study objective

Succes-rate of discontinuation is higher with more gradual tapering of paroxetine or venlafaxine

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

We compare two active tapering strategies

Contacts

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Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria: • Age 18-75 years • Stable 6-month remission of MDD • Confirmed >6 months use of paroxetine (PAR) or venlafaxine (VLX) • Previous MDD episode and current remission confirmed with semi-structured psychiatric interview (MINI).

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 • Insufficient mastery of Dutch language.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Dose comparison
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	01-03-2022
Enrollment:	200
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO Date:	09-08-2022
Application type:	First submission
Review commission:	METC VU medisch centrum
	BS7, kamer H-443 Postbus 7057 1007 MB Amsterdam 020 4445585 metc@vumc.nl

Study registrations

Followed up by the following (possibly more current) registration

ID: 55952
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL9867
Other	ZonMW : 10140021910006
EudraCT	2021-006108-34

Register	ID
CCMO	NL79723.029.22
OMON	NL-OMON55952

Study results

Summary results
tba