Netherlands study of Optimal, PERsonalized Antidepressant use

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To examine in depressed patients who reach a stable depression remission during optimal AD treatment: 1) whether discontinuation is possible; 2) when discontinuation is possible; and 3) in whom discontinuation is possible.

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

Summary

ID

NL-OMON47941

Source
ToetsingOnline

Brief title
OPERA-DISCONTINUATION

Condition

- Mood disorders and disturbances NEC

Synonym
depression, depressive symptoms

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: antidepressants, depression, discontinuation

Outcome measures

Primary outcome

Primary outcome involves sustained remission time measured as time of follow-up without severe depressive symptoms, inpatient admission for depression and suicide (attempt). Severe depressive symptoms are defined as having an IDS score>25 (moderately/severely depressed) and meeting DSM-5 criteria for MDD for 2 weeks according the psychiatric MINI interview. Suicide attempt is assessed using suicide IDS and MINI items followed up with the suicide behaviour question of the Columbia Suicide Severity Rating Scale (C-SSRS) Screen Version) and should be confirmed by two OPERA-researchers.

Secondary outcome

Secondary outcomes concern functioning, quality of life, severity of mood, anxiety and somatic (e.g. side-effects and withdrawal) symptoms and (cost) effectiveness.

Study description

Background summary

Over 1 million Dutch persons currently get an antidepressant (AD) prescribed, with depression as the main indication. Research shows that maintenance treatment after depression remission can decrease relapse. However, long-term AD use can also result in disturbing side effects, medicalization, reduced autonomy and contrasts with preferences of most patients. Current treatment guidelines state that AD use should be continued until at least 6 months after remission to reach a stable depression remission. However, after this period,

it is not clear whether, when and in whom discontinuation of ADs is possible.

Study objective

To examine in depressed patients who reach a stable depression remission during optimal AD treatment: 1) whether discontinuation is possible; 2) when discontinuation is possible; and 3) in whom discontinuation is possible.

Study design

Double-blind placebo-controlled trial in which 400 patients are randomized (1:1) to early discontinuation versus later discontinuation. The trial is complemented with a non-randomized *external reference* patient group to evaluate internal validity and generalizability of the trial sample and study outcomes.

Intervention

The early discontinuation group receives 8 weeks tapering of antidepressants (either citalopram or sertraline, respectively between 10-40 and 50-200 mg/day) + 48 weeks placebo. The later discontinuation group receives 28 weeks AD continuation + 8 weeks tapering + 20 weeks placebo.

Study burden and risks

Burden of participation involves the time spent on study assessments. An extensive baseline assessment will be conducted face-to-face at the field centers. Follow-up assessments after 14, 28, 42, 56 weeks will be face-to-face at the field centres to conduct standard psychiatric interviews in all subjects, provide tablet strips, and allow for overall safety checks on general health of subjects. Follow-up assessments after 7, 21, 35, 49, 80 and 104 weeks will be done online (or through written questionnaire if preferred by subjects). Additionally, during the first year of follow-up, we will monitor depressive and suicidal symptoms, possible withdrawal symptoms and medication adherence regularly with quick online assessments in-between the regular face-to-face and online assessments (at 3.5, 10.5, 31.5 and 38.5 weeks). In those patients who indicate (very) severe depressive symptoms (IDS>25) at an assessment, either a face-to-face or a phone psychiatric interview (MINI-MDD) will follow to assess presence of DSM-5 MDD diagnosis. In those patients who indicate suicidal ideation at an assessment, a (phone) interview (MINI-MDD and C-SSRS Screener Suicide behaviour section) will follow to determine the presence of suicidal behaviour. Both these assessments will also allow for overall safety checks on general health of subjects.

We do not expect an increased risk of participation in the study compared to treatment in routine clinical practice. Discontinuation of antidepressant after

stable depression remission is already indicated in current treatment guidelines and will be conducted in line with these guidelines. Antidepressant discontinuation can cause withdrawal symptoms and increases the risk of relapse. However, during this study, these risks are not increased compared to discontinuation of antidepressants in routine daily clinical practice.

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

• Having a stable depression remission as evidenced by reporting an IDS score <=21 (i.e. no moderate or severe depressive symptoms) during two consecutive bimonthly assessments and a confirmed absence of a DSM-5 diagnosis of MDD during 6 months, as observed in the OPERA-MONITOR study.
• Use of sertraline (50, 100, 150 or 200 mg/day) or citalopram (10, 20, 30 or

40 mg/day).
• Willing to be randomized and provide written informed consent.

Exclusion criteria

• Earlier inpatient admission for depression.
• History of >3 prior episodes for which treatment was started.
• Overall treatment period with antidepressant for the last depressive episode did last more than 18 months (chronic patients are excluded: in this difficult-to-treat group continuation of antidepressants is recommended as a-priori relapse risk is known to be high).
• Presence of other clinically overt primary psychiatric conditions that warrant different medical attention (earlier confirmed psychosis, schizophrenia or bipolar depression for which medical care has been provided, or alcohol or drug addiction which is currently treated).
• 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:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-05-2020
Enrollment:	600
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Citalopram
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Sertraline
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-07-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-01-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2021
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-001518-40-NL
CCMO	NL70053.029.19