Precision psychiatry: Anti-inflammatory medication in Immuno-metabolic depression

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

Summary

ID

NL-OMON56197

Source
ToetsingOnline

Brief title
INFLAMED

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: Hersenstichting

Intervention

Keyword: celecoxib, depression, inflammation, treatment

Outcome measures

Primary outcome

Primary outcome parameter is mean severity of depression symptoms, as measured with the 30-item Inventory of Depressive Symptomatology - self-report during follow-up.

Secondary outcome

Secondary outcome parameters include amongst others, response on the IDS, remission, anxiety, fatigue, food craving, sleep and adverse side events

Study description

Background summary

Depression is a major driver of disability and related health-care costs.
Available treatment options are far from optimal, with only ~60% response.
Developing effective treatments requires new treatment targets to depression pathophysiology. As the role of (neuro)inflammation in depression is emerging, augmentation of antidepressant treatments with anti-inflammatory drugs such as celecoxib has shown encouraging preliminary results.
However, inflammation is not present in all depressed patients.
Depression is heterogeneous: patients express diverse and sometimes opposing symptoms and biological profiles. We recently introduced the concept of ImmunoMetabolic Depression (IMD), characterized by the clustering of inflammatory/metabolic dysregulations and atypical, energy-related symptoms (hyperphagia, weight gain, hypersomnia, fatigue and leaden paralysis), and present in 30% of cases. Converging evidence suggests that in this subgroup of depression cases, inflammation may exert a crucial pathobiological mechanism, representing therefore an actionable therapeutic target. We will apply IMD as a tool to personalize treatment, by matching depressed subjects with IMD with a targeted anti-inflammatory add-on treatment. We expect that this personalized intervention in subjects with IMD, through a reduction of inflammation, lowers depressive symptoms and associated physical fatigue, while increasing

functioning compared to placebo.

Study objective

This study has been transitioned to CTIS with ID 2024-513907-15-01 check the CTIS register for the current data.

Among patients under treatment for depression, we will select 140 persons with IMD. In this specific group of patients, we will test whether celecoxib add-on (400 mg/d) is more effective than placebo in the treatment of depression through a 12-week double-blind, randomized (1:1), placebo-controlled trial.

Study design

12-week double-blind placebo-controlled randomized clinical trial

Intervention

celecoxib add-on (400 mg/d) vs placebo

Study burden and risks

The first part of the study consists of online questionnaires and a video-interview (1.5h) followed by finger prick blood collection, taking ~1 minutes (phase 1). Only individuals meeting all inclusion criteria are randomized (phase 2) and will have 4 face-to-face meetings at baseline (T0, 2 hrs) and after 2 weeks (T1 ~1 hrs), 6 weeks (T3, 1,5 hrs) and 12 weeks (T6, 1,5 hrs). Face-to-face meetings will include diagnostic interviews, blood pressure and weight assessment and questionnaires, and a blood draw. Optional components include additional blood collection for DNA (baseline), additional blood collection for PMBC (baseline, 12 weeks) and stool sampling (baseline, 12 weeks).At 12 weeks, we additionally perform drug accountability. Online questionnaires are filled out in week 4, 8 and 10 (T2, T4, T5, 15 minutes each). Study medication taken twice daily for 12 weeks from T0 to T6. Celecoxib is a Non-Steroidal Anti Inflammatory Drug (NSAID), commonly used in the treatment of arthritis. NSAIDs in general have been linked to cardiovascular and gastrointestinal side effects, but celecoxib has a favourable safety profile over traditional NSAIDs and has less gastrointestinal events than other NSAIDs. Previous RCTs on MDD reported no major adverse events for celecoxib 400 mg/day on top of antidepressants [10]. Since we will exclude (1) persons with contraindications for use of celecoxib as well as persons aged >65 year, and (2) celecoxib will be administered for a limited time, the risk of serious adverse events is expected to be low. We assume a moderate risk for the risk classification.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
* Age 18-65 years
* DSM-5 diagnosis of MDD confirmed with clinical interview (MINI)
* Currently using pharmacotherapy (SSRI, SNRI, TCA, TetraCA, MAOI, other antidepressants [bupropion, vortioxetine, agomelatine]) and/or psychotherapy. Subjects should be on the current treatment for at least 4 weeks
* IDS score >=26 and a score >=6 on atypical, energy-related symptoms scale from IDS
* CRP>1mg/L
* A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:

o Is not a woman of child bearing potential (WOCBP)
o Is a WOCBP and agrees to use, or is already using, a contraceptive method during the intervention period and up to 1 month after the intervention.
* signed informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
* Contraindications for celecoxib (history of: peptic ulcers, gastrointestinal bleeding, ischemic heart disease, stroke, heart failure, allergic reactions to aspirin/NSAIDs/coxibs; impaired kidney function (creatinine clearance < 30 ml/min); impaired liver function (ALT > 2x upper limit of normal [ULT])
* ECT in the past 3 months
* Being on other psychotropic drugs
* Clinically overt alcohol/drug dependence or other primary psychiatric diagnoses (schizophrenia, schizoaffective, OCD, or bipolar disorder)
* Chronic use of anti-inflammatory drugs and corticosteroids
* Current use of anticoagulants
* Not speaking Dutch

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:	Recruiting
Start date (anticipated):	28-09-2022
Enrollment:	140

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Celecoxib TEVA
Generic name:	Celecoxib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-06-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-05-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	07-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2024
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
EU-CTR	CTIS2024-513907-15-01
EudraCT	EUCTR2021-003850-21-NL
CCMO	NL79765.029.21