ISRCTN88666791 https://doi.org/10.1186/ISRCTN88666791

Implementation of Individualized Medicine: Education, Prediction and Treatment (IndiMedDep)

Submission date
28/02/2014

Recruitment status
No longer recruiting

Registration date
26/03/2014

Overall study status
Completed

Last Edited
26/03/2014

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Patients respond to medication differently depending on age, origin, sex, the other drugs they are taking at the same time and their general health. There is growing evidence that genetic difference caused by normal variations in human genomes is an important and sometimes the main factor in response to medication.
The Estonian Genome Center of the University of Tartu (EGCUT) is assessing the possibility of providing psychiatrists with patient-based information about the mutations occurring in genes that encode enzymes metabolising antidepressants. Providing psychiatrists with metabolism information could help them make treatment decisions. The aim of the study is to assess whether a difference in treatment outcomes is detectable for patients with different metabolism speeds. The treatment will be one of two antidepressants: escitalopram or venlafaxine.

Who can participate?
Patients diagnosed with a depressive episode or recurrent depression and prescribed escitalopram or venlafaxine.

What does the study involve?
If you choose to participate you will attend five visits over a three-month period. At visit 1 we will evaluate your suitability for the study and your initial state, collect a blood sample (for the DNA analysis) and start the antidepressant treatment. At visits 2-4 we will assess the effects of the antidepressant treatment and at visit 5 we will continue to assess the effects of the treatment and upon your request give the results of the genetic analysis.

What are the possible benefits and risks of participating?
This is an observational study. The treatment plan does not depend or change upon participation in the study and will be provided as per standard practice.
Participants are given oral and written information about the study. They are guaranteed

sufficient time to examine the information and the opportunity to ask questions related to the study. The study will require a blood test but this will be done at the same time as blood tests done for other analysis when possible.

Where is the study run from?
The participants will be recruited from the psychiatry outpatient clinic of the Tartu University Hospital and the North Estonia Medical Centre. Genetic analysis will be conducted at the Estonian Genome Center of the University of Tartu.

When does the study take place?
February 2014 to December 2016.

Who is funding the study?
University of Tartu (Estonia).

Who is the main contact?
Helene Alavere, Project manager, helene.alavere@ut.ee
Krista Fischer, Senior researcher, krista.fischer@ut.ee

Contact information

Type(s)
Scientific

Contact name
Prof Andres Metspalu

Contact details
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51010

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

Connection between treatment outcome of patients, whose depression treatment was started according to standard practice with escitalopram or venlafaxine, and mutations in the genes (CYP2C19, CYP3A4, CYP2D6), which encode enzymes that metabolise antidepressants: 3-month blinded observational study

Acronym
IndiMedDep

Study objectives
The primary objective of the study is to describe the connection between the treatment outcome of patients whose depression treatment was started according to standard practice with escitalopram or venlafaxine, and mutations in the genes (CYP2C19, CYP3A4, CYP2D6), which encode enzymes that metabolise antidepressants.
The assumption is that in standard practice difference in treatment outcomes for patients with different metabolism speeds is detectable (in this document the term treatment outcome includes the desired and undesired treatment effects, treatment decisions and compliance to treatment).
Sub-objectives are to investigate the questions
1. What kind of differences in treatment effect appear in groups of different metabolism speed after 2 weeks, 1 month, 2 and 3 months after starting the treatment (observed separately in venlafaxine and escitalopram groups)?
2. What kind of differences in side effects appear in groups of different metabolism speed after 2 weeks, 1 month, 2 and 3 months after starting the treatment (observed separately in venlafaxine and escitalopram groups)?
3. What kind of differences in treatment decisions have appeared in groups of different metabolism speed during 3 months since starting the treatment (observed separately in venlafaxine and escitalopram groups)?
4. What kind of differences in medication adherence have appeared in groups of different metabolism speed during 3 months since starting the treatment (observed separately in venlafaxine and escitalopram groups)?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee of the University of Tartu,12/02/2014, ref. 233/T-13

Study design
Multicentre 3-month blinded observational study of standard practice

Primary study design
Observational

Secondary study design
Multi-centre

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Depressive episode or recurrent depression (F32.1-2 or F33.1-2*)* according to ICD10

Interventions
All participants give a blood sample (10 ml of venous blood), of which genomic DNA is separated in EGCUT's lab according to protocol and genotyping is done based on the TaqMan method. On the basis of their genotypes participants are divided into four groups according to the criteria given in table 3: ultrarapid, extensive, intermediate and poor metabolizers. Analysis is carried out after the biological material has arrived at the EGCUT, no later than 1 week before the patient's 5th visit.

5 visits over a three month period have been scheduled for each patient during the study:

Visit 1 (week 0)
1. Evaluation of the inclusion and exclusion criteria: anamnesis, MADRS
2. Informing the patient, getting an informed consent
3. Collecting the data related to demographics and habits
4. Filling out the questionnaires: CGI, EEK
5. Blood sample for collecting DNA
6. Starting the treatment: escitalopram 10 mg a day OR venlafaxine 75 mg (exception 37.5 mg) a day

Visit 2 (at two weeks), visit 3 (at 4 weeks), and visit 4 (at 8 weeks)
1. Filling out the questionnaires: MADRS, CGI, EEK, MMAS-8
2. Registering changes in the data related to demographics and habits
3. Evaluating treatment side effects
4. Medication registration checks
5. Adjusting the treatment scheme, registering the changes, if needed

Visit 5 (at 12 weeks)
1. Filling out the questionnaires: MADRS, CGI, EEK, MMAS-8
2. Registering changes in the data related to demographics and habits
3. valuating treatment side effects
4. Medication registration checks, if needed
5. Adjusting the treatment scheme, registering the changes, if needed
6. Giving and explaining the results of the genetic analysis to the patient upon the patient's request

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure

Primary outcome measured by MADRS (MontgomeryÅsberg Depression Rating Scale) diagnostic interview with ten questions to evaluate the severity of depressive episodes. Highest score indicates a more severe depression. The score of each question varies between 0 and 6 points, the score of the whole questionnaire between 0 and 60 points. The most common cut-off points of the questionnaire score: 06 normal /symptom absent; 719 mild depression; 2034 moderate depression, over 34 severe depression.

Secondary outcome measures

1. CGI (Clinical Global Impression) evaluates the severity of symptoms, therapeutic effect and treatment efficiency for patients with mental disorders. The Clinical Global Impression Severity scale (CGI-S): scale with seven questions allows the doctors to evaluate the severity of symptoms; score 1 normal, not at all ill; 2 borderline mentally ill; 3 mildly ill; 4 moderately ill; 5 markedly ill; 6 severely ill; 7 extremely ill. The Clinical Global Impression - Improvement scale (CGI-I): scale with seven questions allows the doctors to evaluate the changes in the patient's condition (compared to the state at the beginning of the treatment), score: 1 very much improved; 2 much improved; 3 minimally improved; 4 no change; 5 minimally worse; 6 much worse; 7 very much worse. The Clinical Global Impression - Efficacy index (CGI-EI): includes two sub-scales to allow the doctors to evaluate treatment efficiency; therapeutic effect, score: 1 unchanged to worse; 2 minimal; 3 moderate; 4 marked by side effects; side effects, score: 1 none, 2 do not significantly interfere with patient's functioning, 3 significantly interferes with patient's functioning, 4 outweighs therapeutic effect
2. EEK (Emotional State Questionnaire) subjective self-esteem scale to evaluate the symptoms of depression and anxiety, describe the state of the patients with anxiety- and depressive disorders and observe them dynamically. Patient evaluates the statements on a 5-point scale: 0 never; 1 rarely; 2 sometimes; 3 often; 4 regularly; sub-scale points are summarized in scoring. Sub-scales: anxiety (6 statements/ until score 12); agoraphobia and panic disorder (5/7), depression (8/12), asthenia (5/9), sleep (3/6)
3. MMAS-8 (Morisky Medication Adherence Scale) medication adherence questionnaire consists of 8 questions, the first 7 have yes/no answers (yes=1, no=0). The answer to the last question gives 4,3,2,1 or 0 points, accordingly. The points are added up and the patient's medication adherence is evaluated according to their score (8= good medication adherence, 67= intermediate medication adherence and less than 6= poor medication adherence).
4. Registering medications prescribed and purchased (medication, dose, quantity and date) according to the data in the Digital Prescription Center's digital prescription database, the data collector shall write them down into the corresponding form in the study folder. Analogous methodology is currently being successfully used in IndiMed's hypertension study.
5. All possible side effects, their intensity and possible relation to the depression medication are written into the side effects table. Analogous methodology is currently being successfully used in IndiMed's hypertension study.
6. Changes in the treatment scheme (drug change, dosage changes, additional medications, non-regular visits to the psychiatrist/family doctor, hospitalization) are registered according to a form developed for this study.
Measuring complicating factors
7. Questionnaires of EGCUT's state of health and genealogical records (http://www.geenivaramu.ee/documents/egcutquestionnaire.pdf) are used, which have been customized for this study.
8. Depressive episode, recurrent depression and anxiety disorder are diagnosed by the attending physician based on their professional expertise and experience according to the RHK-10 diagnosis criteria on the basis of the patient's anamnesis, examination, and interview conducted with the patient; in case of anxiety EEK anxiety subscale is used additionally (see measuring the outcome)
9. MADRS see measuring the outcome

Overall study start date
20/02/2014

Completion date
31/12/2016

Eligibility

Key inclusion criteria
1. Patient has been diagnosed with depressive episode or recurrent depression (F32.1-2 or F33.1-2* according to ICD10)
2. Depressive episode with at least moderate severity must be specified with MADRS point scores (20 points or more)
3. Patients age 1865
4. Patient has not received medicinal treatment with antidepressants at least in the last 3 months
5. According to the attending physician's assessment the patient needs ambulatory treatment for depression with escitalopram or venlafaxine
6. Patient gives an informed consent to participate in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
300 patients are included in the study

Key exclusion criteria
1. Patient has an additional mental disorder (excluding anxiety disorder), that according to the attending physician's evaluation may affect the patient's medication response to antidepressant treatment or affect the patient's participation in the study in some other way
2. Patient has additional severe recurring physical illnesses, that are not in remission and/or their treatment scheme has changed during last 3 months, and which according to the attending physician's evaluation may affect the patient's medication response to antidepressant treatment or affect the patient's participation in the study in some other way
3. Systematic psychotherapy has been started on the patient within the last 3 months
4. To the knowledge of the attending physician, a close relative of the patient participates in the study
5. Sample formation: sequential patients matching the inclusion criteria, who come to the appointments of the doctors participating in the study

Date of first enrolment

20/02/2014

Date of final enrolment
31/12/2016

Locations

Countries of recruitment
Estonia

Study participating centre
Estonian Genome Center
Tartu
Estonia
51010

Sponsor information

Organisation
Archimedes Foundation (Estonia)

Sponsor details
Koidula 13a
Tallinn
Estonia
10125

Sponsor type
Research organisation

Website
http://archimedes.ee/sihtasutus/

ROR
https://ror.org/02pagex14

Funder(s)

Funder type
University/education

Funder Name

University of Tartu (Estonia)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration