# Clinical trial results:
# The treatment of traumatized refugees with Setraline versus Venlafaxine - a randomized trial.

## Summary

| | |
|---|---|
| EudraCT number | 2011-006228-19 |
| Trial protocol | DK |
| Global end of trial date | 01 October 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 July 2021 |
| First version publication date | 03 July 2021 |
| Summary attachment (see zip file) | Summary, PTF3 (Summary, PTF3.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | PTF3 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01569685 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | The Danish Data Protection Agency: RHP-2012-07, The Danish Ethics Comittee: H-3-2012-020 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Competence centre for Transcultural Psychiatry |
| Sponsor organisation address | Maglevaenget 21, Ballerup, Denmark, 2750 |
| Public contact | CTP, Competencecenter for Transcultural Psychiatry, 0045 38645178, charlotte.sonne@regionh.dk |
| Scientific contact | CTP, Competencecenter for Transcultural Psychiatry, 0045 38645178, charlotte.sonne@regionh.dk |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 31 May 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 September 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 October 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To investigate whether or not there is a difference in the treament effect of Venlafaxine and Sertraline on PTSD symptoms in traumatized refugees.

Protection of trial subjects:

Information was given orally and in writing to each trial subject regarding risks and possible side effects in participating in the study. In the information given, participants were strongly urged to tell their doctor of any side effects, when taking the medication. The most common side effects of the medicines was mentioned, and then the written information was explained. The written information was read aloud by the interpreter and the patients were given the opportunity to ask any questions he/she might have. If a patient did not wish to participate in the study, he/she was offered treatment independently of the trial. If new knowledge was generated during the trial, patients was informed of this, e.g. regarding the effect and side effects of the treatment.

Background therapy:

Cognitive behavioral therapy, following a manual.

Evidence for comparator:

There was limited knowledge about the treatment effect in the patient group, and as there is insufficient knowledge about which of the treatments offered to the patients is the best. Moreover, all patients was given treatment as part of the trial. in addition to the above, it would be unethical to continue to give patients long-term and expensive treatment, if the effect of it is not known. Due to the very limited evidence in this area, this would be the case, if no attempts were made to create evidence on the treatment effect.

| | |
|---|---|
| Actual start date of recruitment | 01 April 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 18 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Denmark: 207 |
| Worldwide total number of subjects | 207 |
| EEA total number of subjects | 207 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |

| | |
|---|---|
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 207 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patient were recruited at Competence center for Transcultural Psychiatry, Psychiatric Centre Ballerup, Denmark from April, 2012 to september 2013. The participant had to be over 18 years old, refugees or reunified with a refugee, have symptoms of PTSD, been previously traumatized, motivated for treatment and having signed informed consent.

### Pre-assignment

Screening details:

The screening for eligible patients to participate began in april, 2012, and the estimated enrollment were 190 patients.

### Period 1

| | |
|---|---|
| Period 1 title | overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Assessor[1] |

Blinding implementation details:

Neither doctors nor patients were blinded in this study, while the raters administering the Hamilton Depression Scale (HAM-D) and the Hamilton Anxiety Scale (HAM-A) were blinded to the time of the interview (so that the raters did not know whether it was a pre-treatment or post-treatment interview) and to the intervention group

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Sertralin |

Arm description:

oral administration- treatment of depression

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Sertraline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

SERTRALINE
CAS number: 79617-96-2
EV Substance Code: SUB10499MIG
Strength
Concentration unit: mg milligram(s)
Concentration type: up to
Concentration number: 200
The IMP contains an
Active substance of chemical origin: Yes

| | |
|---|---|
| **Arm title** | Venaflaxin |

Arm description:

Oral administration- treatment of depression.

| | |
|---|---|
| Arm type | Active comparator |

| | |
|---|---|
| Investigational medicinal product name | VENLAFAXINE HYDROCHLORIDE |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Product name: Venlafaxin
Pharmaceutical form: Capsule, hard
Specific paediatric formulation: No
Routes of administration for this IMP:
Oral use
CAS number: 99300-78-4
Other descriptive name: VENLAFAXINE HYDROCHLORIDE
EV Substance Code: SUB05087MIG
Strength
Concentration unit: mg milligram(s)
The IMP contains an
Active substance of chemical origin: Yes

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Neither doctors nor patients were blinded in this study, while the raters administering the Hamilton Depression Scale (HAM-D) and the Hamilton Anxiety
Scale (HAM-A) were blinded to the time of the interview (so that the raters did not know whether it was a pre-treatment or post-treatment interview)
and to the intervention group

| **Number of subjects in period 1** | Sertralin | Venaflaxin |
|---|---|---|
| Started | 109 | 98 |
| Completed | 109 | 98 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Sertralin |
| Reporting group description: | |
| oral administration- treatment of depression | |
| Reporting group title | Venaflaxin |
| Reporting group description: | |
| Oral administration- treatment of depression. | |

| Reporting group values | Sertralin | Venaflaxin | Total |
|---|---|---|---|
| Number of subjects | 109 | 98 | 207 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 109 | 98 | 207 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 44.0 | 43.2 | |
| standard deviation | ± 9.7 | ± 9.6 | - |
| Gender categorical | | | |
| there were 61 males who recieved venaflaxine and 63 males who recieved sertraline. there were 124 men in total who participated in the trial. | | | |
| Units: Subjects | | | |
| Female | 46 | 37 | 83 |
| Male | 63 | 61 | 124 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Mixed model analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Differences between posttreatment and pre-treatment ratings were analysed using a mixed model, which for each outcome included intervention group, rating time (pre-treatment vs. posttreatment) and the interaction between intervention group and time as predictors.<br>please see table 2 | |

| Reporting group values | Mixed model analysis | | |
|---|---|---|---|
| Number of subjects | 195 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 207 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Gender categorical | | | |
| there were 61 males who recieved venaflaxine and 63 males who recieved sertraline. there were 124 men in total who participated in the trial. | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Sertralin |
| Reporting group description: | |
| oral administration- treatment of depression | |
| Reporting group title | Venaflaxin |
| Reporting group description: | |
| Oral administration- treatment of depression. | |
| Subject analysis set title | Mixed model analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Differences between posttreatment and pre-treatment ratings were analysed using a mixed model, which for each outcome included intervention group, rating time (pre-treatment vs. posttreatment) and the interaction between intervention group and time as predictors.<br>please see table 2 | |

### Primary: Harvard Trauma Questionnaire

| | |
|---|---|
| End point title | Harvard Trauma Questionnaire[1] |
| End point description: | |
| The primary outcome measure was self-reported PTSD symptoms assessed using part IV of the Harvard Trauma Questionnaire (HTQ). Please see attached papers for results of secoundary outcome measures | |
| End point type | Primary |
| End point timeframe: | |
| pra and post-treatment | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: please see attached for statistical analyses

| End point values | Sertralin | Venaflaxin | Mixed model analysis | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 104 | 91 | 195[2] | |
| Units: scale points | | | | |
| arithmetic mean (standard error) | 3.24 (± 0.04) | 3.18 (± 0.05) | 0.09 (± 0.08) | |

Notes:

[2] - the significance of group differences in the difference between pre- and post treatment ratings.

| | |
|---|---|
| **Attachments (see zip file)** | 2016_Sonne, Carlsson, Bech, Elklit, Mortensen_Treatment of |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| September 2012 to October 2014 | |
| Adverse event reporting additional description: | |
| All adverse events were reported during the trial period. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | Excel |
| Dictionary version | 7 |

| Reporting groups | |
|---|---|
| Reporting group title | all groups |
| Reporting group description: | |
| all groups | |

| Serious adverse events | all groups | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 207 (2.90%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Renal cancer | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| bypass operation | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| COPD | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| admission psychiatric unit | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain | Additional description: pain in legs | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| **Non-serious adverse events** | all groups | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 67 / 207 (32.37%) | | |
| Injury, poisoning and procedural complications | | | |
| Injury | | | |
| subjects affected / exposed | 8 / 207 (3.86%) | | |
| occurrences (all) | 8 | | |
| Cardiac disorders | | | |
| Chest pain | | | |
| subjects affected / exposed | 4 / 207 (1.93%) | | |
| occurrences (all) | 4 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 207 (1.93%) | | |
| occurrences (all) | 4 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal discomfort | | | |
| subjects affected / exposed | 12 / 207 (5.80%) | | |
| occurrences (all) | 12 | | |
| Dry mouth | | | |
| subjects affected / exposed | 6 / 207 (2.90%) | | |
| occurrences (all) | 6 | | |
| Gastrointestinal disorder | Additional description: bleeding | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Bleeding anovulatory | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 207 (0.97%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin disorder | | | |
| subjects affected / exposed | 3 / 207 (1.45%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain | | | |
| subjects affected / exposed | 8 / 207 (3.86%) | | |
| occurrences (all) | 8 | | |
| Oedema | Additional description: oedema in legs | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 15 / 207 (7.25%) | | |
| occurrences (all) | 15 | | |
| Metabolism and nutrition disorders | | | |
| Weight increased | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/27825327

http://www.ncbi.nlm.nih.gov/pubmed/27251179

http://www.ncbi.nlm.nih.gov/pubmed/23663588