



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
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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 Committee: 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 treatment 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
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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	Sertraline

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
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Arm description:

Oral administration- treatment of depression.

Arm type	Active comparator
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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			
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			
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. please see table 2	

Reporting group values	Mixed model analysis		
Number of subjects	195		

Age categorical			
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			
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. 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 secondary 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
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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
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Dictionary used

Dictionary name	Excel
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Dictionary version	7
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Reporting groups

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