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Clinical study to assess the efficacy and safety of Silexan in patients with depression

Submission date
21/10/2020

Recruitment status
No longer recruiting

Registration date
01/12/2020

Overall study status
Completed

Last Edited
17/06/2024

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims?
Depression affects people in different ways and can cause a wide variety of symptoms. They range from lasting feelings of unhappiness and hopelessness, to losing interest in the things you used to enjoy and feeling very tearful.
Silexan® is an essential oil produced from fresh Lavandula angustifolia flowers by steam distillation. Clinical trials have demonstrated Silexan to be efficacious and safe in anxiety disorders. The objective of the study is to obtain data on efficacy of Silexan in treating patients with a major depressive disorder of mild to moderate severity.

Who can participate?
Adult male and female patients (aged over 18 years) with mild to moderate depression can participate in the study.

What does the study involve?
One group of patients will receive 80 mg Silexan for 8 weeks. The other groups will take a placebo or 50 mg Sertraline instead. During the study, the severity of the symptoms of the disease will be measured using established scales after 1, 2, 4, 6 and 8 weeks of treatment. The scales are either self-reported or will be assessed by a trained rater. Thereafter, the medication is tapered within one week.

What are the possible benefits and risks of participating?
The participants who receive verum can expect an improvement of their depression. There is no evidence available from the current information on the substance’s ingredients of an unfavourable benefit-risk-ratio.

Where is the study run from?
The study will be performed in selected centres (medical practices) in Germany.

When is the study starting and how long is it expected to run for?
October 2020 to July 2023

Who is funding the study?
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Who is the main contact?
Dr. Stephan Klement
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
750203.01.002

Study information

Scientific Title
Multi-centre, double-blind, placebo- and reference-controlled, randomised trial to prove the efficacy and safety of Silexan (WS®1265) in patients with a major depressive episode of mild to moderate severity

Study objectives
The rationale of this trial is to evaluate the clinical efficacy and safety of 80mg Silexan (WS® 1265) once daily in patients with an acute episode of a major depressive disorder of mild to moderate severity and to demonstrate superiority of 80 mg/day Silexan once daily vs. placebo using the selected rating scales MADRS, BDI-II, CGI, PHQ-9, SDS and (BSS)-5-Item Screen

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/10/2020, Ethikkommission bei der Ärztekammer Niedersachsen (Karl-Wiechert-Allee 18-22, 30625 Hannover, +49 511 380 2208; ethikkommission@aekn.de), ref: 36/2020

Study design
Multi-center randomized placebo- and reference controlled double-blind parallel phase III study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Mild to moderate major depressive episode

Interventions
Patients will be randomly allocated to receive either:
1 x 1 capsule with a daily total of 80 mg Silexan (WS® 1265) and 1 x 1 capsule Sertraline placebo OR
1 x 1 capsule with a daily total of 50 mg Sertraline and 1 x 1 capsule Silexan placebo OR
1 x 1 capsule Silexan placebo and 1 x 1 capsule Sertraline placebo/day
The two capsules (double-dummy) daily will be taken in the morning for 56 days. The treatment phase is followed by a down-titration phase for 7 days, where the capsules are taken every second day. Within the trial sites, the patients' medication numbers are sequentially allocated in the order of inclusion in the randomised treatment period.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Silexan Sertraline

Primary outcome measure

Depression measured using the Montgomery-Asberg-Depression Rating Scale (MADRS total score) at baseline and week 8

Secondary outcome measures
At baseline and week 8:
1. Depression measured using single items of the MADRS
2. Depression measured using Beck depression inventory (BDI-II) total score
3. Clinical Global Impressions of severity of disorder (CGI Item 1) as an organized global assessment of severity conducted by the investigator
4. General health measured using the patient health questionnaire (PHQ-9) total score
5. Sheehan disability (SDS) total score for the documentation of social functioning
6. Clinical global impression of change from baseline (CGI Item 2) as an organized global assessment of change from baseline conducted by the investigator at week 8

Safety outcomes:
1. Rate of patients who discontinue the randomized treatment prematurely due to inefficacy or intolerability
2. Rate of subjects suffering from a (serious) adverse event or a (serious) adverse drug reaction during the treatment phase or the post treatment exposure phase
3. Rate of subjects with item 10 of MADRS > 0 at any individual visit
4. Rate of subjects with Beck Scale for Suicide Ideation (BSS)-5-Item Screen total score > 0 at any individual visit
5. Laboratory values from blood and urine test:
5.1. At the first visit:
5.1.1. Haematology: erythrocytes, platelets, haemoglobin, haematocrit, leucocytes
5.1.2. Metabolites: creatinine, glucose, TSH; Liver enzymes: ASAT (SGOT), ALAT (SGPT), gamma-GT
5.1.3. Coagulation: prothrombin time (PTT), thromboplastin time (Quick), fibrinogen
5.1.4. Electrolytes: sodium, potassium
5.1.5. Urinalysis: protein, glucose, blood
5.2. At visits 2, 3, 5 and 7: Electrolytes: sodium, potassium
5.3. At the last visit:
5.3.1. Liver enzymes: ASAT (SGOT), ALAT (SGPT), gamma-GT
5.3.2. Metabolites: creatinine
6. Vital signs: blood pressure (mmHg), heart rate (bpm) measured using 12-lead ECG at baseline and week 8
7. Physical examination by the researcher to identify potential abnormalities at baseline and week 8

Overall study start date
16/10/2020

Completion date
05/07/2023

Eligibility

Key inclusion criteria
1. Age of at least 18 years
2. Diagnosis of a major depressive episode according to ICD 10 (single episode: F32.0, 32.1, recurrent episode: F33.0, 33.1) of mild to moderate intensity

3. MADRS total score for the inclusion in the run-in and into the acute treatment phase: 19 - 34
4. Out-patient treatment by a general or specialized physician
5. BMI between 18 and 35 kg/m²
6. Written informed consent in accordance with the legal requirement
7. Readiness and ability on the part of the patient to comply with the physician's instructions and to fill in the self-assessment scales

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
498 randomized patients

Total final enrolment
577

Key exclusion criteria
1. Participation in a further clinical trial at the same time or in the last 12 weeks before screening
2. Diagnosis of MDD of severe intensity as defined by ICD-10 (single episode: F32.2, recurrent episode: F33.2) or rating of the MADRS total score >34 at baseline visit
3. Any clinically important psychiatric or neurological diagnoses according to ICD-10, other than study indication, within 6 months before the study
4. History or evidence of alcohol and/or substance abuse or dependence, particularly of sedatives, hypnotics and anxiolytics (F10- F19)
5. Risk of suicide, or previous suicide attempt or clear display of auto-aggressive behaviour as defined (but not limited to) MADRS item 10 "suicidal thoughts" score ≥1 and or a (BSS)-5-Item Screen score ≥1
6. Lack of response to any adequate antidepressant therapy in the present episode of depression or lack of response to Sertraline in any previous episode. Patients who are already well adjusted to an antidepressant therapy in the present episode may not be enrolled into this study
7. Any of the following treatments within 30 days before baseline visit: Antidepressants, depot neuroleptics, MAO inhibitors, pimozide, benzodiazepines, other psychotropic drugs, intravenous methylene blue, linezolid
8. Unacceptability to discontinue or likelihood to need medication during the study that is prohibited as concomitant treatment. The following medication is not allowed during the study: any psychotropic drugs, long-term prophylactic treatment (e.g. lithium, carbamazepine), central-acting antihypertensive medication (guanethidine, guanoxan, clonidin, prazosine, α-methyldopa, reserpine), digoxin, xanthine derivatives such as Theophylline, antiparkinson medication, phytopharmaceuticals with anxiolytic properties, muscle relaxants, analgesics of opiate type, anaesthetics, barbiturates, nootropics, coumarin derivates
9. Non-medicinal psychiatric treatment during the last two weeks prior to baseline visit and

during the course of the study
10. History of hypersensitivity to Lavender preparations or Sertraline and/or known allergies to the IMP, placebo or excipients
11. Any unstable acute medical disorder or clinically relevant hepatic, renal, cardiovascular, respiratory, cerebrovascular, metabolic disorder or progressive diseases as cancer, haematologic diseases or thyroid insufficiency, epilepsy or a history of seizure disorder or treatment with anticonvulsants for epilepsy or seizures, Parkinson’s disease
12. Any somatic disease that necessitate regular treatment with systemic steroids
13. Medical history of angle-closure glaucoma or untreated anatomical "narrow angles" in any eye
14. Medical history of syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatremia in the laboratory analysis at visit 1
15. Clinically significant abnormality of ECG and/or laboratory value
16. Any abnormal baseline finding considered by the investigator to be indicative of conditions that might affect study results
17. Positive pregnancy test during visit 1
18. Pregnancy, planning of pregnancy or lactation
19. Patients capable of childbearing if not using adequate contraception, depending on the gender of the patient the respective contraception applies to their partners during the trial period
20. Gastrointestinal disorders with uncertain absorption of orally administered drugs
21. Unable to read, understand and/or complete questionnaires
22. History or suspicion of unreliability, poor cooperation or non-compliance with medical treatment

Date of first enrolment
30/10/2020

Date of final enrolment
01/11/2021

Locations

Countries of recruitment
Germany

Study participating centre
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Sponsor information

Organisation

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Sponsor type
Industry

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https://ror.org/043rrkc78

Funder(s)

Funder type
Industry

Funder Name
Dr Willmar Schwabe GmbH & Co. KG

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/06/2024

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/04/2024	17/06/2024	Yes	No