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XanaCIDD: A clinical study in which participants are randomly assigned to take either active drug or placebo (non active) to assess if the drug Xanamem is safe, tolerable and effective in helping adult patients with cognitive impairment due to depressive disorder

Submission date
04/03/2023

Recruitment status
No longer recruiting

Registration date
24/08/2023

Overall study status
Completed

Last Edited
20/08/2026

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
This study will test the safety and tolerability (how well the body tolerates) of Xanamem in adults with clinical depression, with ongoing symptoms of low mood and some difficulty with thinking or memory. The study will also test the effectiveness (how well it works) of Xanamem on symptoms that happen with depression, such as sadness and loss of pleasure, tiredness, loss of energy, and difficulty concentrating and thinking.

Who can participate?
The study will take place at up to 4 sites in the UK, as well as 11 sites in Australia. Approximately 160 participants aged 18 – 70 years with major depressive disorder will take part in the study.

What does the study involve?
Participants will be assigned by chance to 1 of 2 treatment groups of equal size - Xanamem or placebo. Neither the participants, the study doctor, or the sponsor of the study will know which group participants are in (called a randomised, double-blind study). Participants will take part in the trial for up to 14 weeks. This includes a screening period of up to 4 weeks, a treatment period of 6 weeks, and a follow-up period of 4 weeks. Participants will have several safety tests done at visits to the study site, such as checking blood pressure and heart rate, physical examination, and blood tests. They will also take several questionnaires and tests to measure their thinking and memory.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration

Risks:
Potential risks of participation for subjects are identified as:
Very common (10% of people tested or more, or at least 10 in 100)
• Headache
Common (between 1% and 10% of people tested, or 1 in 100 to 10 in 100)
• Nausea (feeling unwell)
• Diarrhoea
• Fatigue (tiredness)
• Dizziness
• Tingling in hands or feet
• Joint stiffness
• Back pain
• Blood test indicating mild irritation to the liver (raised ALT)
• Reduced number of nerve fibres in a skin biopsy sample, analysed under a microscope.

Because the investigational product (Xanamem) is at an early stage of development, there may be as yet unknown side effects. However, Xanamem has been previously given to people as single and multiple daily doses up to 70 mg (7 times higher than the doses in this research project) in earlier studies and has been given to over 300 people, including healthy people and people with mild dementia due to Alzheimer's disease. There were no serious, severe, or life-threatening events due to Xanamem treatment. The majority of AEs reported to date were mild or moderate in severity. All AEs will be monitored to resolution and subjects will be encouraged to contact the site if any unexpected events occur between study visits.

In addition to their routine care, subjects choosing to participate in the study will be required to attend the required visits at the study centre. Efforts will be made to schedule the visits to minimise any inconvenience to subjects.

As part of their participation, subjects also will be required to complete the required questionnaires and other diagnostic instruments. Subjects will be able to take reasonable rest breaks, or assessments may be rescheduled to another day, if they become fatigued during the assessments. Subjects are also required to undergo additional study specific procedures as described in the protocol and made known to subjects in the informed consent document. This includes the risk of skin irritation from the ECG patches and bruising, swelling or bleeding from blood collection, for which a topical local anaesthetic cream will be offered if required.

Where is the study run from?
Axiom Real-Time Metrics (UK)

When is the study starting and how long is it expected to run for?
February 2023 to August 2024

Who is funding the study?
Actinogen (Australia)

Who is the main contact?
Dr Stuart Ratcliffe, stuartratcliffe@stpancrasclinical.com

Contact information

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Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05657691

Clinical Trials Information System (CTIS)

2023-000030-15

Integrated Research Application System (IRAS)
1007376

Central Portfolio Management System (CPMS)
56832

Protocol serial number
ACW0008

Study information

Scientific Title
XanaCIDD: A double-blind, randomized, placebo-controlled, parallel-group trial to assess the safety, tolerability, and efficacy of Xanamem® in adults with cognitive impairment due to depressive disorder

Acronym
XanaCIDD

Study objectives
Primary objective:
To determine the effects of Xanamem on attention, including working memory.

Secondary objective:
To determine the effects of Xanamem on depressive symptoms. To determine the effects of Xanamem on executive function. To determine the effects of Xanamem on episodic memory.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/08/2023, Wales REC 1 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 1792 606334; Wales.REC1@wales.nhs.uk), ref: 23/WA/0069

Primary study design
Interventional

Study design
Interventional double-blind randomized parallel-group placebo-controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cognitive impairment due to depressive disorder

Interventions

ACW0008 is a Phase II, randomized, placebo-controlled, parallel-group, double-blind, proof-of-concept trial involving subjects with a confirmed diagnosis of MDD and who continue to experience cognitive impairment and depressive symptoms.

Subjects are assigned at 1:1 ratio to receive either a single dose of 10mg Xanamem or Placebo orally each day.

Subjects will take part in the trial for up to 14 weeks. The trial consists of a Screening period (maximum 4 weeks), treatment period (6 weeks), and follow-up period (4 weeks).

During the treatment period, participants and all personnel involved with the conduct and interpretation of the trial will be blinded to treatment codes. To conceal the blind, Investigational product and Placebo are identical in appearance and dispensing of trial drug will be coordinated by a Randomization and Trial Supply Management system (RTSM). The system will assign a bottle number corresponding to the randomization arm.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Xanamem

Primary outcome(s)
Attention and working memory is measured using digital tests from a cognitive test battery (CTB) (Detection, Identification, and One Back tests) at Screening, Baseline, Week 2, Week 4, Week 6, Week 10

Key secondary outcome(s)
Measured at Screening, Baseline, Week 2, Week 4, Week 6, Week 10, unless otherwise noted:
1. Depression measured using the Montgomery-Åsberg Depression Rating Scale (MADRS)
2. Executive Function is measured using a digital and paper and pencil cognitive tests (One Back Test, Category Fluency Test [CFT], Letter Fluency Test [LFT], and International Digit Symbol Substitution Test - Symbols [IDSST-S])
3. Episodic Memory is measured using a digital and paper and pencil cognitive tests (One Card Learning and Hopkins Verbal Learning Test – Revised [HVLT-R], Immediate Recall only)
4. Individual tests of the CTB including Cogstate tests and other cognitive tests (HVLT-R, CFT, and LFT)
5. The responder rate will be measured by the percentage of participants achieving a 50% or greater reduction in MADRS score and Percentage of participants achieving a MADRS score of < 10 points at Week 6 (EOT)
6. Durability of cognitive and anti-depressive Xanamem effects will be measured by comparing scores 4 weeks after receiving last dose of trial drug (Week 6 vs Week 10)
7. Subjective clinical significance will be measured by the Patient's Global Impression of Severity scale (PGI-S)
8. Subjective clinical improvement will be measured by the Patient's Global Impression of Improvement scale (PGI-I) at week 6
9. Safety and tolerability will be measured by:
9.1. Incidence and severity of treatment emergent adverse events (TEAEs)

9.2. Incidence of SAEs and suspected unexpected serious adverse reactions (SUSARs)
9.3. Clinically significant changes from Baseline in:
9.3.1. Clinical safety laboratory evaluations
9.3.2. Vital signs
9.3.3. Physical examinations
9.3.4. Columbia-Suicide Severity Rating Scale (C-SSRS)
10. Sparse pharmacokinetic sampling for use in PPK analysis at weeks 2, 4, 6
11. Visual Attention and Executive Function will be measured by the Trail Making A and B Tests at screening, baseline, week 6
12. Sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI) at baseline, week 6
13. Assess the effect of Xanamem on trial participant perception of pain using the Brief Pain Inventory at baseline, week 6

Completion date
01/08/2024

Eligibility

Key inclusion criteria
1. Male or female aged 18 to 70 years, inclusive at the time of Screening.
2. Positive MDD primary diagnosis confirmed by MINI at Screening.
3. Persistent depressive symptoms as determined by a HAM-D ≥ 17 at Screening.
4. Self-reported subjective cognitive dysfunction, as determined by an affirmative response to any aspect of a single-question test about perceived problems with their thinking.
5. On a stable dose of a first- or second-line antidepressant that is approved for the treatment of depression (but not a tricyclic antidepressant, monoamine oxidase inhibitor, or vortioxetine) drug for at least 6 weeks.
6. Exhibit a 0.5 SD impairment on the BASIC Boxfiller subtest relative to age, education, and gender relevant norms at Screening.
7. Body mass index (BMI) 17.5 to 38 kg/m2 inclusive at the time of Screening.
8. Must provide written informed consent to participate in the trial and be willing and able to comply with the requirements of the protocol and complete all trial visits.
9. Smokers of ≤ 5 cigarettes a day or equivalent nicotine (includes vaping) / tobacco products are eligible if they are willing to abstain from nicotine / tobacco products on the cognitive testing days.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
167

Key exclusion criteria
1. Active suicidal ideation (“yes” to any of questions 3, 4, or 5 on the C-SSRS and/or per Investigator assessment).
2. On a tricyclic antidepressant, monoamine oxidase inhibitor, esketamine, or vortioxetine.
3. Other comorbid psychiatric disorder of clinical concern, as determined by medical history and Screening assessments.
4. A history of clinically diagnosed dementia of any type.
5. A history of severe depression treated with electroconvulsive therapy.
6. Treatment with transcranial magnetic stimulation within the previous 3 months.

Date of first enrolment
15/12/2022

Date of final enrolment
19/04/2024

Locations

Countries of recruitment
United Kingdom

England

Australia

Study participating centre
St. Pancras Clinical Research Ltd.
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Sponsor information

Organisation
Axiom Real-Time Metrics

Funder(s)

Funder type
Industry

Funder Name
Actinogen

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/07/2026	20/08/2026	Yes	No