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STAND Trial: exploring the feasibility of a cannabinoid oral spray for the treatment of behavioural symptoms in dementia in UK care homes

Submission date
29/10/2020

Recruitment status
No longer recruiting

Registration date
06/01/2021

Overall study status
Completed

Last Edited
09/06/2025

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
People living with dementia often feel agitated or anxious, which can lead to episodes of aggression. This impacts their quality of life and everyday activities, and can cause undue distress & potential harm both to them and those caring for them. Unfortunately, current drug treatments for these symptoms do not work very well and have considerable unwanted side-effects. Recently, early studies have suggested that cannabinoid-based medications could be an effective & safer novel treatment. Further, we want to explore the feasibility & acceptability of a licensed cannabinoid-based medicine, Sativex®, in nursing homes for the treatment of agitation & aggression in Alzheimer's dementia.

Who can participate?
Participants aged 55 - 95 residing in UK care homes in Greater London, living with Alzheimer's Disease, and experience significant & regular anxiety, agitation and/or aggression.

What does the study involve?
Over 4 weeks, participants will either receive Sativex® (a cannabinoid based medicinal oral spray) or a dummy drug. With validated questionnaires, novel data collection methods & interviews with residents and their carers, we will assess the acceptability and impact of Sativex® in nursing homes at every 2 weeks. And finally, we will repeat the assessments 4 weeks after the treatment to explore any potential longer term impact.

What are the possible benefits and risks of participating?
Benefits:
If the treatment is effective for the target symptoms, in the active treatment group it could potentially:
- reduce behavioural symptoms such as agitation & aggression
- reduce pain
- enhance quality of life

- increase appetite
- improve quality of sleep
More broadly, this study will inform our understanding of the acceptability of cannabinoid medications in the dementia and nursing home community. It will explore the feasibility of an oral spray method of administration and whether we can conduct a larger confirmatory trial. Moreover, if this is found to be an effective alternative drug, it may reduce the use of other more harmful drugs that are currently used to manage these symptoms.

Risks:
Known adverse drug-drug interactions will be eliminated during the screening process (incl/excl criteria). The most common side effects reported with Sativex® are increased dizziness (leading to a higher risk of falls), dry mouth, euphoria and sedation. Moreover, we will mitigate these risks by:
a) Dizziness/falls: conducting a risk assessment for falls, explicitly stating in the drug dispensing diary to be aware of fall risk following administration, suggesting that drug be administered when the participant is sedentary (e.g. with meal and tea/coffee times)
b) Dry mouth: asking that refreshment be readily available to all participants following administration (e.g. tea/coffee/juice/water)
c) Euphoria: care staff will be warned that participants may experience euphoric symptoms so that they are not surprised by the reaction
d) Sedation: the risk of sedation will be mitigated by administering the drug in a sedentary position.
Not related to reaction to the drug, participants may have bloods taken before and after the treatment period. A qualified and experienced physician will conduct these procedures, so clinical risk will be extremely low. However, if complications occur, the study team will adhere to appropriate GCP & HTA regulations in response and recommend emergency actions for the participant if needed.

Where is the study run from?
Institute of Psychiatry, Psychology & Neuroscience (IoPPN), King’s College London & South London & Maudsley NHS (SLaM) trust (UK)

When is the study starting and how long is it expected to run for?
September 2019 to September 2022

Who is funding the study?
Alzheimer's Research UK

Who is the main contact?
Mr Chris Albertyn, STAND-trial@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mr Chris Albertyn

ORCID ID
https://orcid.org/0000-0002-4682-6890

Contact details
Institute of Psychiatry, Psychology & Neuroscience (IoPPN)
16 De Crespigny Park
London
United Kingdom
SE5 8AF
+44 (0)207 8480626
Chris.albertyn@kcl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2020-001056-17

Integrated Research Application System (IRAS)
272703

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 45104, IRAS 272703

Study information

Scientific Title
A randomised feasibility trial investigating Sativex® for the treatment of the agitation and aggression (A/A) in Alzheimer's dementia

Acronym
STAND

Study objectives
To determine the feasibility & safety of Sativex® in the treatment of agitation & aggression in Alzheimer's dementia in UK care homes

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/08/2020, West Midlands - Coventry & Warwickshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8009; coventryandwarwick.rec@hra.nhs.uk), ref: 20/WM/0210

Study design
Interventional randomized controlled trial with qualitative follow up

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Dementia

Interventions
Trial design overview:
We propose a double-blind, parallel-group, randomised, placebo-controlled trial (RCT) of Sativex® versus placebo to reduce Agitation and aggression symptoms in Alzheimer's Disease in a nursing home population. This design mirrors the potential future confirmatory phase III trial.

Participants will be randomised to either 'Treatment as usual' (TAU) + Placebo; or TAU + Sativex® for 4 weeks. We plan to recruit 60 patients, and randomisation will be in a 1:1 ratio.

Participants will follow the following regimen for Sativex® [2.7mg (THC)/2.5mg (CBD) per spray] or placebo:
Week 1, Days 1 and 2: 1 spray in afternoon
Week 1, Days 3 to 7: 1 spray in afternoon, 1 spray in evening
Week 2: 1 spray in afternoon, 2 spray in evening
Weeks 3 and 4: 1 spray in morning, 1 spray in afternoon, 1 spray in evening

The primary aim is to assess the feasibility & acceptability of Sativex for this indication in this population using a mixed-methods approach. We will also 'estimate' efficacy outcomes on key neuropsychiatric symptoms, cognition, pain, quality of life and frailty. In-depth semi-structured interviews will be conducted on a sub-sample, estimated to be N=20. Combining quantitative and qualitative methods will provide us with a rich dataset to inform potential progression to a phase III confirmatory trial.

Prospective participants will primarily be recruited from our existing Care Home Research Network (CHRN), consisting of ~200 'research ready' care homes with demonstrated experience of previous trials. See https://www.maudsleybrc.nihr.ac.uk/research/clinical-disorders/dementia/care-home-research-network/. Other recruitment options will be sought as appropriate with key stakeholders and care home networks.

The protocol has been developed in collaboration with our dementia research Public & Patient Inclusion (PPI) groups, and will be continuously consulted throughout the trial and dissemination. The protocol has been independently externally reviewed as part of a competitive grant application process with Alzheimer's Research UK In total, the project will take approximately 2 years to complete.

The 'Participant Experience':
1. Prospective participants will be identified by care provider staff (e.g. care home managers) and /or family members who respond to study adverts with the following overview inclusion criteria: diagnosed with Alzheimer's Disease, living in a care home and displaying symptoms of agitation /aggression.
2. 'Pre-screening': Upon contacting the STAND study, a team member will arrange a pre-screening phone call with the care home. In this call, the study team will confirm: eligibility, mental capacity, and appropriate consenting procedure (ie obtain directly from the prospective participant or seek a legal representative as outlined in the consenting procedure section). A screening visit will ONLY be booked once legal representative consent received, or seeking

consent directly from the individual.
3. 'Screening': A study researcher and the study doctor will visit the nursing home in person to confirm mental capacity status, conduct formal clinical procedures for eligibility (ie physical examination, blood tests), and confirm all other eligibility criteria. The study doctor will also complete a risk assessment for falls as this is the most common side effect of the treatment. If the participant successfully passes these checks, they will be enrolled into the study and the study doctor will co-sign the consent form. A copy of the consent form will be sent to the legal representative (if appropriate), kept in the nursing home, sent to the participants GP, and the original kept securely with the study team.
4. 'Baseline' (day 0): A study researcher will complete all assessments as outlined in the protocol for baseline metrics, including assessments directly with the participant, a key worker who knows the participant well, and broad care home level information. For a sub-sample (N=20), the study researcher will conduct a semi-structured interview with the key worker.
5. 'Randomisation & delivery of drug/placebo' (day 0/1): Following baseline, the participant will be randomized into either the 'treatment' or 'placebo' arm of the study. Once randomised, the study researcher will collect the drug/placebo from the pharmacy and deliver to the nursing home (researcher will be 'blind' to the allocation). They will include a drug dispensing diary, drug administration guidelines and witness the first administration in person.
6. 'Mid-point safety check' (day 14): a study researcher will visit the care home to conduct CMAI, NPI-NH and check for adverse events & compliance issues. They will also deliver the actigraphy wrist-watch to be worn by the participant for the remaining 2 weeks of the intervention period.
7. 'End of intervention visit' (day 28)': a study researcher & study doctor will visit the home and conduct all procedures as specified in the protocol. They will also collect the actigraphy wristwatch, remaining drug/placebo and diary card.
8. 'Post-intervention safety phone call' (day 42): a study researcher will call the nursing home to carry out a safety check for adverse events, and conduct the CMAI and NPI-NH.
9. 'Final study visit' (day 56): a study researcher will conduct a final visit to the nursing home and conduct the assessments as specified in the protocol. Here they will also conduct a 'closing interview' with the sub-sample involved in the qualitative evaluation.

Participants will therefore only be expected to be in the study for 8 weeks (+ time to screen). Participants will be exposed to a relatively small portion of study assessments, with other assessments being conducted with a staff proxy informant who knows them well. Interviews with the sub-sample can be conducted via telephone or in-person depending on requirements.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Feasibility outcome measures:
1. Number of participants recruited measured using case report forms at the end of the study
2. Number of participants followed up measured using case report forms at the end of the study
3. Medication adherence measured using case report forms at the end of the study

Key secondary outcome(s))

1. Safety and tolerability:
1.1. Tolerability: Assessed by self- & carer-report of side-effects, medication discontinuation, Co-prescribed psychotropic medications, and number of occasions rescue treatment utilised throughout the study
1.2. Safety parameters:
1.2.1. Blood samples for Haematology (Full red & white blood cell count and Haemoglobin) and Biochemistry (Urea, liver function test, thyroid function test, lipid profile) measured at baseline and 4 weeks
1.2.2. Vital signs: Heart rate and Blood pressure; Physical examination measured at baseline and 4 weeks
1.2.3. Follow up phone calls for self-reported side effects, including incidence of falls and compliance (week 2 and 6)

2. Neuropsychiatric symptoms, cognition, pain, quality of life measured at baseline and again where indicated:
2.1. Cohen-Mansfield Agitation Inventory (CMAI) at 2, 4 & 8 weeks at daily dose
2.2. Neuropsychiatric Inventory – Nursing Home (NPI-NH) 2, 4 & 8 weeks
2.3. Mini Mental State Examination (MMSE) 4 & 8 weeks
2.4. Functional Assessment Staging of Alzheimer's Disease (FAST) 4 weeks
2.5. Clinical Frailty Scale (CFS) 4 weeks
2.6. Quality of Life with resident 4 & 8 weeks (QOL-AD care home)
2.7. Quality of Life with proxy informant 4 & 8 weeks (QAULID)
2.8. Pain; Abbey Pain Scale (APS) at 4 weeks

3. Qualitative sub-study outcomes of interest measured using semi-structured interviews at baseline and 8 weeks:
3.1. Attitudes towards cannabis-based medicines
3.2. Issues/benefits of administering via an oromucosal method in this population
3.3. Feasibility and acceptability of wearables in the population
3.4. Factors of regular care home activities/procedures that may facilitate or inhibit effective implementation of Sativex® in practice

Completion date
04/09/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/05/2022:

1. Age 55 - 95 years
2. Probable Alzheimer's Disease diagnosis according to the criteria of National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDSADRDA)
3. Clinically significant A/A that requires treatment, defined by CMAI >/= 45 and/or NPI-NH Agitation total score >/= 4
4. Residential within a nursing home at recruitment to the study with a history of at least 2 weeks behavioural disturbance
5. Written and witnessed informed consent from participant (if deemed having mental capacity), or from personal legal representative (next of kin/power of attorney), or from professional legal representative (non R/F member who can attest to knowing prospective participant for

significant period of time). Informed consent will be sought in this order from these potential sources

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Previous inclusion criteria:

1. Age 55 - 90 years
2. Probable Alzheimer’s Disease diagnosis according to the criteria of National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDSADRDA)
3. Clinically significant A/A that requires treatment, defined by CMAI >/= 45 and/or NPI-NH Agitation total score >/= 4
4. Residential within a nursing home at recruitment to the study with a history of at least 2 weeks behavioural disturbance
5. Written and witnessed informed consent from participant (if deemed having mental capacity), or from personal legal representative (next of kin/power of attorney), or from professional legal representative (non R/F member who can attest to knowing prospective participant for significant period of time). Informed consent will be sought in this order from these potential sources

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Current exclusion criteria as of 24/05/2022:

1. Anti-psychotic, anti-epileptic, antidepressant, benzodiazepine, lithium or hypnotic dosage alteration in the 2 weeks prior to the start of the study (and must be expected to maintain dosage throughout study).
2. ChEIs (donepezil, rivastigmine or galantamine) and/or memantine, dosage alteration in the 6 weeks prior to the start of the study.
3. Currently using cannabis-based medicine(s) (defined as being a UK licensed product prescribed by a doctor)
4. Concomitant treatment with strong enzyme inducers (rifampicin, carbamazepine, phenytoin, phenobarbital, St John’s Wort) and/or CYP3A4 inhibitors
5. Hypersensitivity to Sativex® or any of the excipients in the formulation (ethanol anhydrous,
6. Propylene glycol, peppermint oil).
7. Severe cardiovascular disease, recent myocardial infarction (‘recency’ determined by study doctor according to clinical significance), uncompensated congestive heart failure and uncontrolled hypertension.
8. QT interval by Fredericia (QTcF) greater than 450 will be excluded if ECG conducted

9. Severe, unstable or poorly controlled medical illness.
10. If diagnosed with severe kidney disease/impairment (as deemed by study doctor/PI), a blood test (taken within 12 months) is required to assess severity of renal impairment: Renal Impairment is defined by estimated Glomerular Filtration Rate (eGFR) less than 45ml/min
11. If diagnosed with severe liver disease/impairment (as deemed by study doctor/PI), a blood test (taken within 12 months) is required to assess severity of hepatic impairment: Hepatic impairment is defined by Alanine aminotransferase (ALT)/ Aspartate aminotransferase (AST) levels 3 times greater than reference value of laboratory (165 IU/L+ for ALT; 150 IU/L+ for AST)
12. Any disability that may interfere with the patient completing the study procedure.
13. History or family history of schizophrenia, or other psychotic illness; history of severe personality disorder or other significant psychiatric disorder other than depression associated with their underlying condition.
14. Delirium, pain or any medical illness as a clear cause of agitation
15. Females of child-bearing potential, defined as 'having experienced menarche and are not permanently sterilised (e.g. by hysterectomy, bilateral salpingectomy and bilateral oophorectomy) or post-menopausal (defined as at least 1 year since last regular menstrual period)'.
16. Evidence of 'suicidality risk' determined by >0 on Columbia-Suicide Severity Rating Scale (CSSRS)
17. History/current seizure disorder
18. History/current of alcohol or other substance abuse
19. History of fall(s) within the last 6 months

Previous exclusion criteria:

1. Anti-psychotic, anti-epileptic, antidepressant, benzodiazepine, lithium or hypnotic dosage alteration in the 2 weeks prior to the start of the study (and must maintain dosage throughout study)
2. ChEIs (donepezil, rivastigmine or galantamine) and/or memantine, dosage alteration in the 6 weeks prior to the start of the study
3. Currently using cannabis-based medicine(s) (defined as being a UK licensed product prescribed by a doctor)
4. Concomitant treatment with strong enzyme inducers (rifampicin, carbamazepine, phenytoin, phenobarbital, St Johns Wort) and/or CYP3A4 inhibitors
5. Hypersensitivity to Sativex® or any of the excipients in the formulation (ethanol anhydrous, Propylene glycol, peppermint oil)
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7. QT interval by Fredericia (QTcF) greater than 450 will be excluded if ECG conducted
8. Severe, unstable or poorly controlled medical illness
9. Renal Impairment as defined by estimated Glomerular Filtration Rate (eGFR) less than 45ml /min
10. Hepatic impairment as defined by Alanine aminotransferase (ALT)/ Aspartate aminotransferase (AST) levels 3 times greater than reference value of laboratory (165 IU/L+ for ALT; 150 IU/L+ for AST)
11. Any disability that may interfere with the patient completing the study procedure
12. History/current diagnosis of schizophrenia or other psychotic illness, history of severe personality disorder or other significant psychiatric disorder
13. Delirium, pain or any medical illness as a clear cause of agitation
14. Females of child-bearing potential, defined as 'having experienced menarche and are not

permanently sterilised (eg by hysterectomy, bilateral salpingectomy and bilateral oophorectomy) or post-menopausal (defined as at least 1 year since last regular menstrual period)'
15. Evidence of 'suicidality risk' determined by >0 on Columbia-Suicide Severity Rating Scale (C-SSRS)
16. History/current seizure disorder
17. History/current of alcohol or other substance abuse
18. History of fall(s) within the last 6 months

Date of first enrolment
01/08/2021

Date of final enrolment
04/07/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College London
Institute of Psychiatry, Psychology & Neuroscience (IoPPN)
16 De Crespigny Park
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
Alzheimer’s Research UK; Grant Codes: ARUK-GCTF2018B-001

Alternative Name(s)
Alzheimer's Research Trust, AlzheimersResearch UK, AlzResearchUK, ARUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

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		31/05/2025	09/06/2025	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 4.0	07/02/2022	24/05/2022	No	Yes