Sativex® for the Treatment of AgitatioN in Dementia ('STAND') trial

This study will explore a cannabinoid-based medicine (Sativex®) for the treatment of behavioural symptoms in people with Alzheimer's disease in nursing homes.

Please take time to read the following information carefully and discuss it with others if you wish. Before you decide to take part in this research study, it is important for you to understand why the research is being done and what it will involve.

Please ask a member of the study team if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part. There is no requirement to participate, and you may withdraw at any time. If you decide to take part, we would be delighted if you sign and return the corresponding consent form to us, and you may keep this information sheet.

Full title of research:

A randomised feasibility trial investigating **S**ativex® for the **T**reatment of the **A**gitatio**N** & Aggression (A/A) in Alzheimer's **D**ementia. ('STAND' trial).

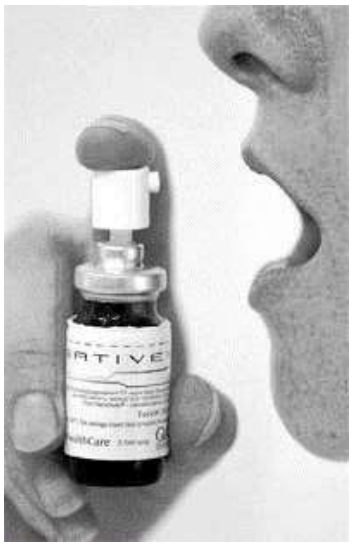
Why are we doing this study?

People living with dementia often feel agitated or anxious, which impacts their quality of life and everyday activities, causing undue distress 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 in dementia.

Why are we inviting you to participate?

We believe that you are part of a group who live in care homes that would potentially benefit from Sativex® to help with feelings of anxiety and agitation. In order to find out whether Sativex® is acceptable in nursing homes, we are inviting individuals like you to take part in a research project in which people will be given either Sativex® or a placebo equivalent so that we can compare.

What is Sativex®?



- Sativex is a mouth spray which contains cannabis extracts called cannabinoids (50% delta-9-tetrahydrocannabinol (THC), 50% Cannabidiol (CBD)).
- It is currently licensed for use in used in multiple sclerosis (MS) to improve symptoms related to muscle stiffness. This is also called "spasticity".
- Early evidence has suggested that both THC & CBD could be beneficial for behavioural and psychological symptoms of dementia, with a combined approach potentially being most effective.
- More detailed information can be found here: https://www.medicines.org.uk/emc/product/602/pil.

What is involved?

Once you have had a chance to discuss, ask questions and think, the researcher will ask you to consent to take part by signing a consent form. Following signing the consent form, and confirming you meet all eligibility criteria, you will be enrolled into the study.

After an initial baseline visit, you will be randomly assigned to receive Sativex® or a placebo (a matched spray for comparison that has no pharmacological effect) for a period of 4 weeks. As it is random, study researchers will have no control over which allocation you receive. Also, as a 'double-blind' study, study researchers, care home staff and yourself will not be aware of whether you receive Sativex® or placebo for the duration of the study. If you are unhappy with the possibility of potentially receiving a placebo, you should not take part.

Each week, the dose will gradually increase to a maximum dose of 4 sprays per day (1 in the morning, 1 in the afternoon, and 2 in the evening). Over the 4 weeks of the treatment period, we will ask you to wear a wristwatch monitor so that we can track your sleep and physical activity. We will visit the care home regularly 5 times over a period of 8 weeks to conduct assessments with you and your caregivers about how you are doing and how you are handling the new medication. The flow chart on the following page provides an overview of all study procedures.

Note: Apart from the consent form and contact details, all personally identifiable information will remain in the care home. All information collected by researchers will be anonymised.

Screening ('Pre-study start') – signed consent received before or during this visit

- A qualified doctor and study researcher will conduct a **physical exam** of yourself, examine your **medical history & curent medications**, and **discuss with care home staff** to determine if it is safe and appropriate for you to enrol in the study.
- If deemed necessary, the doctor will ask your GP for recent blood results, or if unavailable, to take a blood sample to examine your underlying biochemistry (including liver and kidney function).

Baseline visit ('Day 0')

A study researcher will book an appointment with you to visit or video call to:

a) briefly **interview you & your carers** with questionnaires to collect information about your health and well-being.
b) be given **access to your care plan and medical records** to collect information about your medical history, medications and typical standard of care.

c) **talk with the care home manager/staff** to get more broad information about the care home.
d) **deliver a wrist-worn watch monitor** so that we can observe yourphysical activity and sleep over the 4 weeks of the treatment. Please keep this on for the entire 4 weeks.

Randomisation & Dispensing drug ('Day 1')

Once eligibilty and safety confirmed, a study researcher will:
a) **send letter to GP** to inform them about your enrolment into the trial
b) **randomly assign you** to receive Sativex® or placebo for 4 weeks (50:50). Study reserachers and care home staff will not know which treatment you are on.
c) **deliver the drug/placebo to the nursing home** with instructions & dispensing diary for staff and observe the first dose.

Mid-point visit ('Day 14')

Halfway through the 4 week treatment period, a study researcher will either visit or call to:
a) **Follow-up with care home staff** about how you have been doing and any potential initial impact the treatment has been having, and switch over for a **fresh watch monitor**.

End of treatment visit ('Day 28')

- Similar to the baseline visit, on the last day of your treatment, a qualified doctor and study researcher will conduct a **physical exam** of yourself, examine your **medical history & curent medications**, and **discuss with care home staff** about any potenial impact the treatment may have had for you and for care home practices.
- The doctor will **take a blood sample** so that we can assess the impact on your underlying biochemistry (incldуing liver and kidney function)
- The researcher will collect the remaining drug/placebo, dispensing diary, and wrist-watch monitor.

Post treatment check 1 ('Day 42')

A study reseracher will **call the care home** to check how you have been since the treament, and collected information about your health and well-being.

End of Study final visit ('Day 56')

A study researcher will visit the care home a final time to **ask how you have been since stopping treatment**. This will include accessing your medical history, medication records, care plan, and discussing with care home staff members.

Do I have to take part?

You are free to decide whether you would want to take part in this study or not. If you choose not to take part, this will not affect the care you typically receive. If you do decide take part, you should keep this information sheet and you will be asked to sign a participant consent form. Even if you agree, you are free to withdraw at any time without giving a reason. Please note, if you do decide to participate, alcohol consumption is prohibited during the treatment period, and male participants must use contraception throughout the study and for at least 3 months from the end of treatment period.

Will being in this study help you or others?

It is not yet clear whether participating in this trial will directly benefit you or not. However, it is our sincere hope that this study will help us to understand whether Sativex® is an acceptable & safer future treatment for psychological & behavioural symptoms in dementia.

Are there risks to you in this study?

Sativex® has been reported to be highly tolerated in older individuals. However mild common side effects include:

- Increased dizziness directly after administration
- Dry mouth
- Feeling tired

To mitigate these risks, we will be asking that care home staff only administer the treatment when you are seated, and offer you refreshment as needed. Additionally, obtaining up to 2 blood samples involves an invasive procedure. This procedure will be conducted by a qualified & experienced physician. Further, we hope this will significantly reduce any risk. If any clinically relevant information arises that suggests a risk of harm to you or others (study related or not), we will disclose to your GP for their information.

How will we use your information?

King's College London (KCL) is the lead sponsor for this. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. KCL will keep identifiable information about you for 25 years after the study has finished. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. Your anonymised

research data may be shared with academic partners and non-commercial stakeholders in the future if deemed by the study team that it will significantly progress our understanding of the treatment and/or patient population.

You can find out more about how we use your information by contacting the study team or visiting the KCL website: https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research.aspx.

What will happen to my samples?

After collecting blood samples, they will be delivered to Viapath Laboratory at King's College Hospital. Here, they will conduct analysis of full blood count, lipid profile, and thyroid, kidney and liver function. **Blood samples will be destroyed directly after analysis in the laboratory**. Contact details for the laboratory are:

Contract Research Viapath Laboratory
King's College Hospital
Denmark Hill
London, SE5 9RS
Telephone: 020 3299 3726/5548
Email: kch-tr.ContractRandD@nhs.net

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team via our contact details below
- by contacting King's College London's Data Protection Officer, Mr Albert Chan at info-compliance@kcl.ac.uk

Who is organising and funding the research?

This study is funded by Alzheimer's Research UK (registered charity numbers 1077089 and SC042474).

Led by Professor Dag Aarsland, the study team are based in the Department of Old Age Psychiatry, Institute of Psychiatry, Psychology & Neuroscience, King's College London.

King's College London (KCL) and South London & Maudsley (SLaM) NHS Trust are co-sponsoring this study.

Who has reviewed the study?

The West Midlands – Coventry & Warwickshire Research Ethics Committee (REC) and the Medicines and Healthcare products Regulatory Agency (MHRA) authorised this Clinical Trial.

Will I be paid for my participation in this study?

You will not receive any monetary compensation for your participation in this study.

What if there is a problem?

If you encounter any issues whilst participating in the study, please first contact the research team using the contact details at the end of this form. Additionally, you can also contact the South London & Maudsley (SlaM) NHS Trust Patient Advice & Liaison Service (PALS) via freephone, 0800 731 2864, or email, **pals@slam.nhs.uk.**

Statement about insurance cover

In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against King's College London and/or SlaM NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate). King's College London has obtained insurance which provides no-fault compensation i.e. for non-negligent harm, you may be entitled to make a claim for this.

Contact for Further Information

If you wish to participate, you will be asked to sign a consent form. You can keep the information sheet for your records. Thank you for reading this and for your interest in the study.

If you have any questions or concerns about any aspect of this study, you should ask to speak with the study team who will do their best to answer your questions. They can be contacted by:

Post:
STAND Trial Manager
Department of Old Age Psychiatry
Institute of Psychiatry, Psychology & Neuroscience (6th Floor)
16 De Crespigny Park
London, SE5 8AF

Telephone:

-02078485134 (office)
-07521 902042 (mobile)

Email:

STAND-trial@kcl.ac.uk

Website:
https://www.kcl.ac.uk/academic-psychiatry/about/departments/old-age