Centre for Neuropsychopharmacology
Division of Psychiatry, Dept. of Brain Sciences
Imperial College London
Commonwealth Building, Hammersmith campus
160 Du Cane Road
London W12 0NN
Tel 0207 594 7028

Participant Information Sheet

Title: FORWARDS-1; Evaluating the safety of acute baclofen in methadone-maintained individuals with opiate dependence

Principal Investigator: Prof Anne Lingford-Hughes

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

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of this study?

The primary purpose of the research is to establish the safety of baclofen when taken in combination with methadone.

We believe that baclofen has the potential to help successful opiate detoxification (stopping your methadone gradually) in those who are being prescribed methadone for opiate dependence. However, before we can test this, we need to determine that the doses of baclofen and methadone that are usually prescribed, are safe when taken together. We also need to determine the best dose of baclofen to use.

Why have I been chosen?

You have been chosen to participate because you are currently being prescribed a stable dose of methadone for opiate dependence. We need up to 64 individuals like yourself to complete the study.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You will be

free to withdraw at any time and this will not affect your care. You may be asked the reason for withdrawing to help with future recruitment and for safety purposes, but providing this information is not compulsory.

What will happen to me if I take part?

If you decide to take part please note that you will not be eligible if you feel unwell, or have taken alcohol or drugs of abuse in the previous 24 hours before a study visit.

You will be asked to attend study visits as follows:

Visit 1: a screening visit (2-3 hours), to take informed consent and check your suitability for the study. This will take place at the Imperial Clinical Research Facility (ICRF) in the Hammersmith Hospital, or at the CIPRes clinic at St Charles Hospital.

Visit 2: an experimental visit (6-7 hours) where you will receive baclofen or placebo, after taking your usual dose of methadone. This visit will always take place at the Imperial Clinical Research Facility (ICRF).

We will arrange return transport for all your visits e.g. by taxi. For some screening activities, you may prefer to be seen at your local addiction services within CNWL NHS Trust. This can be arranged where appropriate.

We will also keep in touch via telephone for pre-screening conversations, as well as for contact before your experimental day and to monitor your progress the day after.

Visit 1: screening

After discussion of the study and the consent procedure, screening tests will be performed to decide if you are suitable for the study. These tests will include:

- Questions about your medical, psychiatric, substance and medication use.
- A physical examination including a record of your vital signs, height, weight, blood pressure and pulse.
- An ECG recording. This is a painless way of measuring the activity of the heart.
- An alcohol breathalyser test.
- Urine samples to check for pregnancy and recent use of recreational drugs.
- Some questionnaires about your mood, sleep and drug history.
- A watch to wear that monitors your sleep via wrist or ankle movement (note, this is not a smart watch and does not monitor your location or anything else. It will be returned at the end of the study)

If requested by the doctor, additional tests may include:

- Blood tests (approximately 15ml, which is the same as 3 teaspoons) to ensure that these are within the normal range.
- A respiratory examination to determine your lung function

We will inform your GP or local drug & alcohol service of your planned participation in the study and we may request medical information from them concerning your suitability to

participate, but **we will not share the results of any tests with your clinical team or GP without your permission**.

The visit will take approximately 2-3 hours at a relaxed pace and refreshments will be provided. You will be able to take smoking breaks if required. Transport will be arranged if required.

Visit 2: Study Visit

If the results of the screening visit are satisfactory you will be asked to attend the NIHR Imperial Clinical Research Facility at Hammersmith hospital for the experimental visit, lasting approximately 6-7 hours (with breaks). A taxi will transport you to the research centre in the morning of each study day. We will normally ask you to arrive at around 9-10am and stay until approximately 4-5pm. Please have your usual breakfast before you come.

IMPORTANT: For the study visit, you will be required to bring your usual dose of methadone with you to the study centre where we will observe you taking it. This is important because we need to time the dose of the study medication, baclofen, to occur as soon after your methadone dose as possible. We will help with any arrangements required for you to bring your methadone with you.

The following information will be recorded:

- Urine test for pregnancy or recreational drugs
- Breath test for alcohol
- Medications since your last visit

You will not be eligible if you feel unwell, or have taken alcohol or drugs of abuse in the previous 24 hours.

Once we are happy that you have fulfilled the eligibility requirements we shall start the study procedures. You will take your usual dose of methadone, then, after baseline assessments, you will receive a single dose of orally administered baclofen, or a placebo (dummy pill). We will then monitor you at regular intervals after drug administration, allowing adequate rest/smoking breaks.

Monitoring procedures will be conducted as follows:

- Respiratory measures:
    - blood oxygen saturation- via a finger clip
    - breathing rate- measured via a nasal cannula (a non-invasive tube the sits at the edge of your nose), or a band around your waist
    - blood carbon dioxide levels via a finger clip or nasal cannula
- Sedation measures: measured via rating scales by someone observing your behaviour
- ECG Measures
- Vital signs; blood pressure, pulse, body temperature.
- Questionnaires with pencil and paper or on a computer

- Blood Samples (10ml, ~2 teaspoons). For this, we shall put a small plastic tube into one of your veins (equivalent to an intra-venous drip in hospital) so we can take small blood samples during the day easily.

Please note that if you are unable to provide blood due to e.g. tricky or inaccessible veins, you don't have to do so.

We will repeat these measurements at regular intervals during the day. You will be given a sandwich lunch of your choice. At about 5 hours after dosing, we will check your health and if this is satisfactory you will be allowed home by taxi that we will organise for you. If you are still feeling the effects of the drug, we may ask you to stay until we are happy for you to leave.

Follow-up

We will telephone you the following day after the study to check on your health and arrange for payment.

Compensation

For completing the whole study you will receive £150 in recognition of the time and inconvenience of taking part. You can receive this directly into your bank account, or as vouchers if you prefer. This includes payment of £50 for the screening visit and £100 for the study visit. Travel expenses will be paid. If you fail to complete a study day, you will receive payment on a pro-rata basis, at the discretion of the research team.

What drug is being tested?

On the study visit day, you will be given some tablets to take. These will be either a medication called baclofen or placebo dummy pills. You will not know which you are taking on the study day. This is so that any changes in the measurements we take are not biased by expectation.

From our experience with baclofen, we do not anticipate any issues from these doses. Baclofen has been licensed for many years for the treatment of muscle spasm in people with conditions such as spinal injuries. It is also used to treat people with alcoholism.

What do I have to do?

- Attend the study days, or let us know in plenty of time if you cannot be there.
- Report any changes in your health or medications to one of the study team.
- Not take any alcohol or other illicit substances (including heroin) for at least 24 hours before each study day.

What are the risks of taking part?

There is no risk from any of the measurements we take, except for a slight risk of bruising from the insertion of the plastic tube in your vein when providing blood samples.
Baclofen has been used for many years in a large number of patients. In studies of single doses with healthy volunteers, few side effects have occurred but some subjects have

experienced sedation, particularly at higher doses. Other side effects that have occurred in patients taking the drug regularly are mild gastro-intestinal disturbances such as constipation or diarrhoea, dry mouth, nausea and vomiting, low blood pressure, light-headedness, dizziness, headache, insomnia, increased frequency of urination.

If you have a known contraindication to baclofen, or to any of the contents of either the baclofen or placebo tablets, you will not be eligible to take part.

It is important to test the safety aspects of combining baclofen with methadone because both medications can produce depressant effects on the central nervous system (CNS) when taken separately, particularly at high doses. However, there is no indication of a drug interaction between baclofen and methadone at the doses we will prescribe. Baclofen medication may change the way in which you perceive the effect of your methadone, and we are interested in measuring this change, so it will be assessed as part of the study. Baclofen will not induce any opiate withdrawal.

The clinical interviews may involve discussion of sensitive or triggering issues– but they are relevant to our study of drug dependence. We will be able to provide support and guidance, which will help reduce any worries you may experience.

Pregnant women or those planning to become pregnant cannot take part in this study. Women of childbearing age will be asked to have a pregnancy test before taking part and will be asked to use an effective contraceptive during the course of the study. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her research doctor.

If you currently have private medical insurance, please ensure you check with your provider before agreeing to take part in order to check it does not affect your current medical insurance. We do not expect to uncover any medical condition you may be unaware of, if we do, you will be informed immediately, and the next steps will be discussed with you.

What are the possible benefits of taking part?

You will not benefit from taking part, but the information we get about baclofen will be used to design the next study which may help improve the treatment of people with opiate dependence in future.

What happens when the research study stops?

After taking part, your treatment with the addiction service will continue as in your care plan. When all the participants have completed the study, we will be able to tell you whether you had placebo or baclofen. If you would like to know, please tell us.

How will we use the results of this research?

When we have established the safety parameters for combining baclofen with methadone in this study, we will use the information about the best dose of baclofen to help to design our next study. This will test whether baclofen can help people to detoxify from methadone

in those desiring abstinence. There are currently very few, if any, treatments available to support this in the UK, so this will be an important next step.

In addition, our research investigating new medications for addiction and their mechanism of action includes the study of receptors in the brain which baclofen affects, called GABA-B receptors. We have already done a similar study in non-drug addicted as well as alcohol addicted people, and now need to compare their results with opiate dependent people. We will publish the results of this study in a scientific journal.

What if something goes wrong?

There are always doctors at the research centre who will provide emergency medical cover if required.

You will be given a contact card (the size of a credit card) with details of the study, and emergency contact details to carry with you.

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This provision does not apply to claims which arise as a result of Hepatitis, HIV/AIDS or any related conditions. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Anne Lingford-Hughes, details at the top of this information sheet). The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, 'Research Governance and Integrity Team'.

HOW WILL WE USE INFORMATION ABOUT YOU?

Imperial College London is the sponsor for 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. Imperial College London will keep your personal data for:
10 years after the study has finished in relation to data subject consent forms.
10 years after the study has completed in relation to primary research data.

We will need to use information from you and from your medical records (GP, local drug and alcohol service) for this research project. This information will include your initials, NHS number, name, date of birth and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data (including the samples that we collect) will have a code number instead. We will keep all information about you safe and secure.

It is now common for research data to be shared with others where it is in the public interest to do so. There is a process for data sharing that has to be followed in order to safeguard your personal data. Some of your information may therefore be sent to other institutions, and they must follow our rules about keeping your information safe. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

If you have declined to allow the use of your samples in future research, they will be destroyed at the end of the study, otherwise they will be stored in accordance with the processing of personal data, as detailed above.

If you have agreed to be contacted about future research in the consent form, we will keep a record of your name and contact details. You can ask to be removed from this record at any time.

LEGAL BASIS

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

INTERNATIONAL TRANSFERS

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (**EC**) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

SHARING YOUR INFORMATION WITH OTHERS

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties.

- Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.
- The following Research Collaborators / Partners in the study;

  - Cambridge University – your study ID number will be shared with the trial statistician who is based at Cambridge University. It is shared so that the statistician can add your data to the study database in order to carry out analysis.
  - Other data sharing anonymised data
- Sharing of fully anonymised research data with other researchers can occur. Fully anonymised data does not contain any personal data and the link between your study ID number and your data has been removed.

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. If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

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
- by sending an email to l.paterson@imperial.ac.uk, or
- by ringing us on **0207 5947028**.
- **OPTION** Link to Research website – to be added when complete

COMPLAINT

If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

Confidentiality

All information collected about you will be kept strictly confidential and stored and processed according to the Data Protection Act. To safeguard your rights, we will use the minimum personally-identifiable information possible. We will not share any confidential information, or the result of any tests e.g. urine drug screen, with your GP or clinical team without your permission. However, should there be any concerns about risks of harm to you or anyone else, a clinical decision will be made with regard to disclosure of information and reporting of the risk. In this case, appropriate support will be discussed with you. The research data we collect from you are anonymised, so they can only be identified by a subject number.

Who will have access to my data?

Personal data: Imperial College Healthcare NHS Trust (Hammersmith Hospital) and Imperial College London will collect personal information from you for this research study in accordance with our instructions. The only people who will have access to information that directly identifies you will be people who need to contact you about the research study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, or contact details.

Other information

This study has been approved by the West of Scotland REC-1. It has been reviewed and funded by the Medical Research Council (MRC). The study will follow the ethical principles laid down in the Declaration of Helsinki.

Contact Details

If you have any questions, please do not hesitate to contact the research team at the address provided on page 1. Dr Katie Herlinger, is the study doctor, and can be contacted on [0207 594 7028] during working hours (09:00-17:00) or at [**07745 300960**].

You can also contact the Patient Advice and Liaison Service (PALS) which offers independent advice for your concerns, suggestions and queries. They are available Monday to Friday 9am-5pm on the following number; 02033133322 or at imperial.pals@nhs.net**.**