petra
Pregabalin for treatment resistant generalized anxiety disorder

Participant Information Sheet
Pregabalin for Treatment Resistant Anxiety (PETRA) Study

We invite you to take part in a research study

- We want to find out if the combination of an antidepressant and pregabalin is effective for anxiety where the antidepressant alone has not been very effective.
- If you agree to take part in the research, you will be randomised to either pregabalin or an identical placebo (a "dummy" pill) alongside your antidepressant.
- By completing questionnaires at the beginning and at approximately 3, 6, 12, 26 and 30 weeks after you enter the study we can find out if pregabalin alongside antidepressant medication has been more effective than prescribing antidepressants alone.
- You can stop taking part in the study at any time, without giving a reason.

Important things you need to know:

- Before you decide whether to take part, it is important you understand why the research is being done and what it will involve.
- Please take time to read the following information carefully. Discuss it with friends and relatives if you wish.
- You are free to decide whether or not to take part in this research. If you choose not to take part, this will not affect the care you get from your GP.
- Ask us if there is anything that is not clear or if you would like more information.
- If you decide to take part, please see the attached letter for details of what to do next.

Contents

How to contact us

If you have any questions about this study, please talk to:

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UCL University of BRISTOL Keele UNIVERSITY NHS National Institute for Health Research

1 Why we are doing this study?

What are we studying?

Many people visit their General Practitioner (GP) with excessive, unpleasant worrying or feeling generally anxious, nervous, or tense. This can be called Generalised Anxiety Disorder (GAD) and often occurs alongside depression and low mood. GPs often prescribe antidepressants for worry and anxiety, but about half of people do not experience a reduction in symptoms.

What do we hope to find out?

Pregabalin is an effective anti-anxiety drug when used on its own. We want to find out if a combination of an antidepressant and pregabalin is effective for anxiety where the antidepressant alone has not previously been very effective. The results of the study will let doctors give better advice to people with anxiety who have taken antidepressants but have not found them helpful. We hope around 500 people will agree to take part.

2 How does the study work?

People who agree to take part in the study will be given study medication to take alongside their antidepressant. This medication will either be pregabalin or an identical placebo (a "dummy" tablet) that will not contain pregabalin. Researcher will discuss with you which dose may work for you; this can range from one to four tablets (50-200mg of pregabalin) per day to ensure that you can find the level that works best for you and the side effects are minimised. People will take study medication for 26 weeks. People will then be asked to gradually reduce their medication for up to 28 days to minimise withdrawal effects if they occur.

How is it decided who gets an active drug and who gets placebo?

A computerised process will allocate you to a treatment group – this is called 'randomisation'. It is a bit like rolling dice to decide and it means you have an approximately equal chance of being allocated either pregabalin or the placebo tablets. Neither you nor the research team will know which treatment group you are in.

3 Why am I being asked to take part?

Your GP is involved in the study and thinks it might be of interest to you, as you are currently taking antidepressants.

4 What will happen to me if I take part?

Enrolling you in the study

If you are interested in taking part you will need to either reply directly to us, **or** to ask your GP to refer you into the trial (see the attached letter for more details on what to do next).

The researcher will need to check whether you might be eligible to take part in the study by asking you some questions over the telephone or online.

Not everyone who completes the initial assessment will be suitable to take part in the study, and we will let you know.

Collecting information

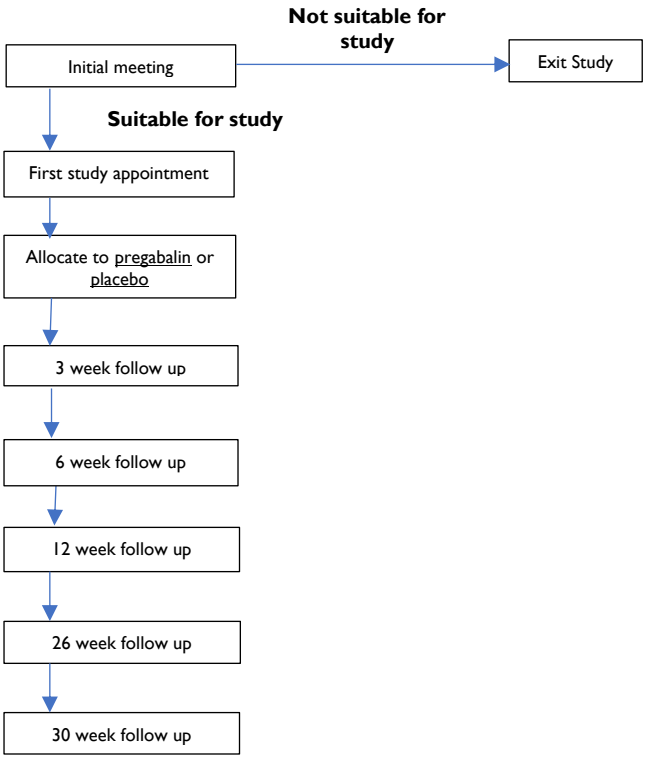
If you want to proceed with the study, we will invite you to attend an appointment that will be either online or face-to-face and it will take about 1 hour and 30 minutes. The researcher will explain the study and answer any questions you may have. You do not have to enter the study

unless you feel completely happy with what you are being asked to do.

You will be asked to complete a consent form, and to answer some more questionnaires. The questions ask about you, your current and past symptoms of anxiety and depression, alcohol use, general health, other stressors and medication. Based on the answers you give; the researcher will tell you whether you are eligible to take part in the study. If you are not eligible, or do not want to take part, you will continue your usual treatment with your GP.

If your answers suggest you are suitable for the study, and you are willing to take part, you will then be randomised (allocated to receive either pregabalin or placebo) and sent the study medication by post.

Follow up



If you take part in the study, we will arrange 5 follow up meetings at 3, 6, 12, 26 and 30 weeks after your first meeting. The follow up meetings can take place online or face-to-face at your home or your GP surgery. You will choose the location. The follow up meetings will take about 40 minutes; you will be asked to complete online questions like those you complete at the first appointment.

At the end of the study, we will give you a short questionnaire about your experiences of taking part.

As part of the consent process, we will ask for your permission for us to have access to your medical notes to collect the number of consultations and prescriptions you have received.

Women of childbearing potential

Pregabalin could be harmful to unborn babies and may be passed to breast milk. Therefore, if you are pregnant or breastfeeding, you will not be able to take part in this study.

If there is a chance you could become pregnant, you will also be asked to take a pregnancy test before starting the trial medication and at the end of the study. If your period is late while taking part in the study you will be asked to take another pregnancy test. You must agree to use highly effective contraception throughout the trial and up to 7 days after stopping the trial medication.

Highly effective contraceptive methods include:

- Combined (oestrogen and progestogen containing) hormonal contraception (e.g. the contraceptive pill, a birth control vaginal ring, patch, or injection).
- Progestogen-only hormonal contraception (e.g. the progestogen-only contraceptive pill, injection, or implant).
- Intrauterine device (IUD) (e.g. the coil) or Intrauterine hormone-releasing system (IUS) (e.g. the coil).
- Bilateral tubal occlusion (e.g. permanent female sterilisation)

- Vasectomised male partner (e.g. permanent male sterilisation)
- Sexual abstinence (abstinence is acceptable only as true abstinence, occasional abstinence and withdrawal are not adequate methods of contraception).

If you become pregnant during the trial, you should inform your doctor immediately and the study medication will be discontinued. We would like to follow the progress of your pregnancy with your consent. We would ask you to provide information including date pregnancy confirmed, estimated date of delivery and estimated gestational age when pregnancy confirmed, the outcome of your pregnancy, if it goes to term and also any antenatal or postnatal problems for up to 8 weeks after delivery. Your participation in providing information is entirely voluntary. If you agree, we will ask you to sign a consent form to show that you have agreed to provide information on your pregnancy. This information might help us to better understand any effect of the study medication on pregnancy and the unborn baby.

Additional 6th Interview

If you take part we may also ask you to consider having a 6th interview with a researcher so you can talk at more length about your views and experiences in the study. This interview is optional, and we will ask for your consent separately. Further information can be found on the specific Information Sheet.

If you agree to be interviewed, this will take place remotely at a time that is convenient for you. The interview will take less than 60 minutes and will be audio-recorded with your consent so that we have an accurate record of the conversation. This is the only interview in the trial that we will record. An encrypted audio recorder will be used and recordings will be transcribed by a transcription company. Only members of the research team will have access to the recorded interview and its transcript. We will remove any identifiable information such as names from the transcript so that you cannot be recognised from it. The transcript will then be stored for use in future research studies and may be shared with other researchers. The recording will be deleted after transcription.

5 How is taking part in the study different from usual GP care?

In usual care, patients would either continue to only take the antidepressant medication or may additionally take other anti-anxiety medication recommended by their doctor. In this study, you will either be taking pregabalin or placebo in addition to your antidepressant. This allows us to make a fair and accurate assessment of whether taking pregabalin alongside the antidepressant is working.

6 What is the drug that is being tested?

The study is investigating pregabalin or placebo taken with your current antidepressant treatment.

Sedation and dizziness are the most common side effects of pregabalin especially at higher doses. You will take between 1 and 4 tablets of study medication per day. Therefore you can reduce the number of tablets if you experience side effects. A full list of all the side effects reported for pregabalin is given at the end of this information sheet.

7 Possible benefits and disadvantages of taking part?

What are the possible benefits of taking part in the trial?

Some people find it rewarding to take part in medical research and appreciate the additional monitoring and contact with the researchers. The results of the study may improve treatment and increase understanding of anxiety for future patients even if you do not directly benefit from taking part.

What are the possible disadvantages and risks of taking part in the trial?

This is a randomised controlled trial therefore you cannot choose which treatment you receive. Your allocation will be decided by chance and neither you, your GP, nor the researchers you meet will know which treatment you are receiving.

Some people experience withdrawal symptoms when they stop pregabalin. After the 26 week interview the amount of study medication you take will be gradually reduced so that withdrawal symptoms are less likely. The final follow-up meeting will be 30 days after the 26 week follow up meeting and we will ask about any withdrawal or other symptoms.

If your anxiety worsens you may be advised to stop the study medication and then ask your GP for advice on further treatment. If you stop your study medication, your GP can find out which study treatment you have taken to give you the best advice.

You can stop taking the study medication at any time. We would ask you to discuss this with your GP (and let us know) so they can advise you and provide any future care. You should not stop the medication suddenly unless advised to do so by a doctor.

Your progress in the study will be monitored by the researchers including the local Principal Investigator who is a clinician. You can contact them on 0207 679 9253 with any questions about the study, your medication or anything else. You can still see your usual GP at any time with any health issues you may be worried about.

Whilst you are a participant in this study UCL will be responsible for all study procedures including the study medication and follow up meetings for the duration of the study.

Some of the assessment questions will ask about low mood and self-harm. Whilst most people do not mind answering these questions, some people may feel upset. You don't have to answer any questions you don't want to. If you become distressed answering these questions or at any point during the study the researcher will offer support by directing you to supportive services. If it appears that you are at imminent risk of harm to yourself or others the researcher will contact your usual GP or other mental health teams as further support might be necessary. The researcher will always aim to discuss this with you first, but this may not always be possible. Where a significant risk is identified, such contact may be made without your permission.

8 More information about taking part

Do I have to take part?

It is up to you to decide whether or not to take part. We will describe the study and go through this information sheet with you. The standard or type of care you receive is not affected if you choose not to take part.

What happens if new information becomes available during the course of the study?

Sometimes during a study, new information becomes available about the treatment being studied. If this happens, the research team will tell you and discuss whether you want to continue in the study. If you decide to stop taking part in the study your usual GP care will continue. If you decide to continue in the study, you may be asked to sign an updated consent form. If we think you should withdraw from the study, we will explain the reasons and arrange for your treatment to continue with your GP.

What happens if the study stops?

Very rarely a study is stopped early. If this happens, the reasons will be explained to you and arrangements made for your GP for your care to continue as usual.

What if there is a problem or you want to complain?

If you have a concern about any aspect of this study, you should ask to speak to the researcher who will do their best to answer your questions.

Every care will be taken during this clinical trial. However, in the unlikely event that you are injured by taking part, compensation may be available. If you suspect that the injury is the result of the Sponsor's negligence (University College London) then you may be able to claim compensation. Complaints can be made by writing to the UCL Joint Research Office (research-incidents@ucl.ac.uk). After discussing with your study doctor, please make the claim in writing to Prof Glyn Lewis (Glyn.Lewis@ucl.ac.uk) who is the Chief Investigator for the clinical trial and is based at UCL. He will pass the claim to the Sponsor and on to the Sponsor's Insurers. If you have a claim, then it might be helpful to consult a lawyer.

Participants may also be able to claim compensation for injury caused by participation in this clinical trial without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your study doctor in the same way as above. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects you may have experienced due to your participation in the study, the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this or details are on the NHS website.

How will we use information about you?

We will need to use information from you for this research project. This information will include your initials, name, date of birth, NHS number, address 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, address or contact details. Your data will have a code number instead.. We will keep all information about you safe and secure.

Only authorised members of the research team will have access to your information though we will need to pass on your name, address and contact details to the pharmacy who will send you the study medication.

Certain individuals from research team and regulatory organisations may occasionally look at your medical and research records in order to meet legal, ethical and safety requirements. All individuals who have access to data will be bound by strict data protection and confidentiality rules. The researchers who analyse the study

information will not be able to identify you or see your name, NHS number or contact details.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports so that no one who takes part in the study can be identified. We will use the information we collect to look at how best to help people with anxiety.

What are your choices about how your information is used?

University College London is the sponsor for this trial and will act as the data controller with Camden and Islington NHS Foundation Trust (C&I), so UCL and C&I are responsible for looking after your information and using it properly. Your personal data collected for the study will be kept for 5 years after the study has finished.

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/ or by visiting our website https://www.ucl.ac.uk/comprehensive-clinical-trials-unit/use-data, contacting CCTU-enquiries@ucl.ac.uk, or contacting the UCL Data Protection Officer at data-protection@ucl.ac.uk. The Comprehensive Clinical Trials Unit (CCTU) is coordinating this study.

What will happen if I don't want to carry on with the study?

If you don't want to carry on with the study, you can leave at any time but it is important that you do not stop taking the study medication suddenly. You will need to gradually reduce your dose as instructed.

We would still like you to complete the follow-up questionnaires if you leave the study so that we can monitor your progress.

Involvement of your GP

We will tell your GP that you are taking part in the study. With your permission, we will inform them of your results on the initial screening questions we use to check if you are eligible to take part.

At the end of your involvement in the study, we will also send your GP information about your treatment allocation and ask you to see your GP for a review. This will help them to plan your ongoing care.

If you tell us you are having thoughts about harming yourself or others, we will need to let your GP know of our concerns. We will of course discuss this with you. In rare situations, if you or someone else is in danger, we might have to contact your GP without your consent.

What will happen to the results of the study?

When the study is completed, the results will be published in a medical journal so that doctors and other health care professionals can read the results. Your identity and personal details will be kept confidential. No named or identifiable information about you will be published in any report about this study. We will also provide you with a summary of our findings from the study.

Who is organising and funding the study?

The study is funded by the National Institute for Health and Care Research (NIHR).

Who has reviewed the study?

The study has been reviewed by an independent group called a Research Ethics Committee and the study has been given a favourable opinion.

9 Contact for further information

If you have any questions regarding the study or how you might be involved further contact information can be found below.

Local researcher

Lauren Harding-Brown
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+447483421893

Chief Investigator

Professor Glyn Lewis Glyn.Lewis@ucl.ac.uk
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In the event of emergency please dial 999, 111, contact your GP if appropriate or go to your local A&E.

Thank you for taking the time to consider taking part in this study.

Full list of possible side effects

Like all medicines, pregabalin can cause side effects, although not everybody gets them. They are also related to the dose that you take, so people taking high doses may be more likely to feel side effects. You should not expect these things to happen to you, but this list shows all the symptoms that patients have said they have had when taking pregabalin which they suspect may be side effects. They are usually mild or short term and go away by themselves.

Very common: may affect more than 1 in 10 people:

- Dizziness
- Drowsiness
- Headache.

Common: may affect up to 1 in 10 people:

- Mood changes.
- Memory problems.
- Blurred vision.
- Vertigo, problems with balance.
- Dry mouth, constipation, vomiting, flatulence, diarrhoea, nausea, swollen abdomen.
- Difficulties with erection.
- Swollen hands, arms, legs and feet.
- Feeling drunk, abnormal style of walking.
- Weight gain because pregabalin can make you feel hungry
- Muscle cramp, joint pain, back pain, pain in limb.
- Sore throat.

Uncommon: may affect up to 1 in 100 people

- Weight loss because pregabalin can make you lose appetite.
- Change in sense of self, restlessness, depression, agitation, mood swings, difficulty finding words, hallucinations, abnormal dreams, panic attack, apathy, aggression, elevated mood, mental impairment,
- Changes in eyesight, dizziness on standing, sensitive skin, loss of taste, burning sensation, tremor on movement, decreased consciousness, loss of

consciousness, fainting, increased sensitivity to noise, feeling unwell.
- Dry eyes, eye swelling, eye pain, weak eyes, watery, or irritated eyes,
- Changes in heartbeat, low blood pressure, high blood pressure.
- Flushing, hot flushes.
- Difficulty breathing, dry nose, nasal congestion.
- Increased saliva production, heartburn, numb around mouth.
- Sweating, rash, chills, fever.
- Muscle twitching, joint swelling, muscle stiffness or pain.
- Breast pain.
- Difficulty with or painful urination, incontinence.
- Weakness, thirst, chest tightness.
- Changes in blood and liver test results.
- Hypersensitivity, swollen face, itchiness, hives, runny nose, nosebleed, cough, snoring.
- Painful menstrual periods.
- Coldness of hands and feet.

Rare: may affect up to 1 in 1,000 people:
- Unusual sense of smell, problems with vision
- Dilated pupils, cross eyes.
- Cold sweat, tightness of the throat, swollen tongue.
- Inflammation of the pancreas.
- Difficulty in swallowing.
- Slowness or reduced movement of the body.
- Difficulty with writing properly.
- Increased fluid in the abdomen.
- Fluid in the lungs.
- Convulsions.
- Muscle damage.
- Breast discharge, abnormal breast growth, breast growth in males.
- Interrupted menstrual periods.
- Kidney failure, reduced urine volume, urinary retention.
- Decrease in white blood cell count.
- Thoughts of harming or killing yourself.
- Allergic reactions which may include difficulty breathing, inflammation of the eyes and serious skin reactions, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms.
- Jaundice (yellowing of the skin and eyes).
- Tremor, decreased ability to move, and muscle stiffness.

Very rare: may affect up to 1 in 10,000 people
- Liver failure, inflammation of the liver.

If you experience swollen face or tongue or if your skin turns red and starts to blister or peel, you should seek immediate medical advice.