

Patient Information Sheet (Study enrolment)

Methylphenidate versus placebo for fatigue in advanced cancer (MePFAC)

You are being invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information.

Please take time to decide whether or not you wish to take part.

What is the purpose of the study?

People who have been treated for cancer often find they experience tiredness or exhaustion (fatigue) that does not improve with rest. It is a widespread problem in people with cancer at all stages of their illness whether they are receiving treatment or not and is particularly common in patients receiving palliative care. There is no "standard" care pathway for the management of cancer-related fatigue and it is not routinely assessed or monitored by healthcare staff in the UK.

The purpose of this study is to determine whether a medication that has mood-enhancing and stimulant properties (Methylphenidate) is effective, in comparison with a "dummy pill" that has no therapeutic properties (a placebo), in the treatment of cancer-related fatigue in patients receiving palliative care. Methylphenidate is currently used to treat children with Attention Deficit Hyperactivity Disorder (ADHD), in whom it has been shown to be a safe and effective medication. There is some reason to believe that it may also help adults with cancer-related fatigue, but it has not yet been adequately investigated for this purpose.

Why have I been invited?

You have been invited because, after being screened, you have been found to be suitable to take part in this study. We are asking 230 patients over the age of 18 who have advanced cancer with moderate to severe cancer-related fatigue and are receiving palliative care to participate in this research.

Do I have to take part?

No, it is up to you to decide whether or not you take part in this study. We will describe the study to you in detail and go over this information sheet. At this point you will also have the opportunity to raise any questions about the study. You do not have to take part unless you feel completely happy with what you are being asked to do. If you agree to take part, we will then ask you to sign a consent form and you will be given a copy. You are free to withdraw at any time without giving a reason. Whether or not you decide to be involved will not affect the standard of care you receive.

What will happen to me if I take part?

If you are found to be eligible to take part in the study you will be invited (usually by phone) to attend for a baseline assessment. This will occur within two weeks of being screened for the study.

At the baseline visit you will be asked to complete a number of questionnaires about your health and your fatigue levels. These will take approximately 20 minutes to complete. You will also have your blood pressure and pulse rate recorded and a researcher will check that there is no other reason why you could not be included in the study. At the end of the baseline visit you will be given either methylphenidate or an identical looking “dummy pill” (placebo). The whole baseline visit will take approximately 60 minutes. Neither yourself nor the medical or research team will know whether you have received the methylphenidate or the placebo. This is to make sure that the study is a “fair test”. Which treatment you receive will be decided randomly by a computer program. You will have a 50% chance of receiving either the methylphenidate or the placebo.

You will be instructed to take one tablet twice daily for at least one week. At the end of the first week, you will be contacted by telephone by one of our researchers. The researcher will ask you some questions about your fatigue, any side-effects you may or may not be experiencing and whether or not you feel that the tablets are helping. The telephone call will last approximately 15 minutes. The researcher will then communicate with your doctor and will call you back with advice about whether to continue on the current dose of the tablets or to change (or stop) the tablets altogether. If the doctor is unsure then they may contact you directly to discuss things further (or to ask to see you again) before making a decision.

You will be contacted again after two weeks on the study tablets and the same procedures will be followed. On the third week you will need to come back to the hospital/hospice to be seen by one of the doctors. At that appointment you will complete the same questionnaires as you did at the beginning of the study and will

have your blood pressure and pulse rate checked again. You will be given another supply of tablets. The appointment will last approximately 45 minutes.

You will be contacted by telephone again after four, five, seven and eight weeks of treatment. After six and nine weeks treatment you will be asked to come back to the hospital/hospice again for further assessments like the one you underwent at the beginning of the study. After each telephone call or visit you will be advised whether to continue on the same dose of the tablets or whether to increase, decrease or stop the tablets altogether. The most tablets that you will be advised to take will be four tablets three times daily. During the last week of the study the dose of the medication will gradually be reduced and at the end of the nine week visit, your involvement in the study will be finished.

Any additional travel expenses that you incur as a result of making additional visits to the hospital will be covered by the research team. Please let your research nurse know if you wish to claim back these expenses.

Are there any disadvantages in taking part?

Like all medicines, methylphenidate can cause side effects, but not everybody gets them. The side-effects are described in the section below.

In addition to the possibility of developing side-effects, involvement in the study may be an added inconvenience for you. You will need to stay in regular contact with the research and clinical team. You will need to be available for a weekly telephone call or visit to the hospital/hospice, and you will need to take the time to answer questions on the phone or complete questionnaires about your health and fatigue levels. You will need to have your blood pressure and pulse monitored when you attend the hospital/hospice.

Do the treatments have any side effects?

Methylphenidate is generally safe when given to children with hyperactivity (ADHD). However, it is not known how safe it is in people with cancer who are experiencing fatigue. There is therefore a risk that you may develop side-effects or complications from the tablets.

Very common side-effects (affecting greater than 1 in 10 people) are; difficulty sleeping; nervousness and headache.

Common side-effects (affecting greater than 1 in 100 people) are; cold or flu-like symptoms; loss of appetite; mood swings; aggression; agitation; anxiety; depression; irritability; abnormal behaviour; dizziness, abnormal movements; hyper-activity;

drowsiness; abnormal heart rhythms; fast heart rate; palpitations; high blood pressure; cough; sore throat; abdominal pain; diarrhoea; nausea; stomach discomfort; vomiting; dry mouth; hair loss; itch; skin rashes; urticaria (raised, red itchy skin bumps); joint pains; fevers; and weight loss.

Uncommon side effects (affecting greater than 1 in 1000 patients) are; allergic reactions such as angioneurotic oedema (swelling affecting lips, tongue, hands, feet, rashes and breathing difficulties); anaphylactic reactions (severe allergic reactions); swelling of the ears; blistering skin conditions; exfoliative (peeling) skin conditions; urticaria (raised, red itchy skin bumps); itch; rashes; psychosis (hearing, seeing or feeling things that aren't really there); anger; suicidal ideas, alteration in mood; mood swings; restlessness; tearfulness; tics (fast, repetitive muscle movements that result in sudden and difficult to control body jolts or sounds); worsening of pre-existing tics or Tourette's syndrome (a neurological condition, characterised by a combination of involuntary noises and movements called tics); hypervigilance (a state of high alert); sleep disorders; sedation; tremors; double vision; blurred vision; chest pain; constipation; abnormalities in liver function blood tests; muscle pains; muscle twitching; blood in the urine; chest pain; fatigue; and heart murmurs.

Rare side effects (affecting greater than 1 in 10,000 patients) are; mania (abnormally elevated mood); disorientation; libido disorder (abnormally high or low sex drive); difficulty focusing vision; dilation of the pupil; visual disturbances; angina (chest pain on exercise); breathlessness; excessive sweating; macular (small flat) skin rashes; erythema (red skin rash); and gynaecomastia (swelling of the breasts in men).

Very rare side-effects (affecting fewer than 1 in 10,000 patients) are; anaemia (lack of red blood cells); lack of white blood cells (thereby increasing risk of infection); lack of platelets leading to easy bruising; suicide attempts or suicide; short-lived depressed mood; abnormal thinking; apathy; repetitive behaviours; over-focussing; fits; involuntary movements; reversible mini-strokes; cardiac arrest; myocardial infarction (heart attack); cerebral arteritis or occlusion (stroke); peripheral coldness; Raynaud's phenomenon (poor blood flow to fingers and toes); abnormalities in liver function; coma due to liver failure; exfoliative (peeling) dermatitis (eczema); erythema multiforme (severe skin rash); fixed drug eruptions (skin lesions which recur in the same area when the same drug is given); muscle cramps; sudden cardiac death; increase in blood alkaline phosphatase or bilirubin level (liver enzymes);

Side-effects about which the frequency is unknown (cannot be estimated from available data) are: lack of all components in blood (red cells, white cells and platelets); delusions; thought disturbances; confusion; drug abuse and drug dependence (addiction); excessive incoherent and uncontrollable talkativeness; problems with blood circulation in the brain leading to stroke; fits; migraines; abnormal heart rhythms (fast and slow rhythms, extra beats); dry skin; difficulty obtaining or

maintaining erections; priapism (persistent erections); chest discomfort; very high temperatures

All side-effects will be listed on the leaflet accompanying the treatment when prescribed and your doctor will be happy to discuss these with you. You will also be given a telephone number to contact the research team if you are concerned.

A member of the research team will be in contact with you every week (either by telephone or at a face-to-face visit) and will closely monitor you for any side-effects. If any side-effects are detected then this information will be communicated to the clinical and research team and appropriate actions will be taken. This may include reducing or stopping the study medication or other interventions to address specific problems.

What are the possible benefits of taking part?

If the methylphenidate is effective, then there may be some benefit in terms of reducing your fatigue. Some people may also find that their fatigue improves even if they are given the “dummy pills” (placebo).

Some people find it reassuring to be in regular (weekly) contact with a member of the research or clinical team for the duration of the trial.

It is important to remember that we cannot promise that the study will help you. However the information that we get from this study may help improve the treatment of other people with cancer related fatigue. We will ensure that your treatment is delivered to the highest clinical standard and quality standards and we will be monitoring your progress throughout.

What are the alternatives for treatment?

No other medicine has consistently been proven to be effective for cancer-related fatigue. Patients who experience cancer-related fatigue are usually advised to take regular aerobic exercise and to maintain a healthy diet.

What if relevant new information becomes available?

Sometimes we get new information about the treatments being studied. We don't think this is very likely to be the case, but if it happens, we will tell you about it and discuss whether you want to, or should, continue in the study. If you decide not to carry on, we will make arrangements for your care to continue. If you decide to continue in the study we will ask you to sign an updated consent form. If the study is stopped for any other reason, we will tell you why and arrange your continuing care.

Will my GP be informed of my involvement?

With your permission, your GP, and other doctors who may be treating you, will be notified that you are taking part in this study.

Will my taking part in this study be kept confidential?

Yes. All information collected about you during the study will be kept strictly confidential and in accordance with the Data Protection Act 1998.

So that we can keep in contact with you during the study it will be necessary to share your personal details (name, address, date of birth, telephone number, medical history) with members of the research team. This is so that we can safely advise you about the dose of medication to take. We will also need to share your personal details with the NHS Information centre so that we can keep a track of what happens to you after your involvement in the study. The other forms that we use to record your information will not contain your name but will instead use your initials, date of birth and trial identification number, to minimise any risk to confidentiality.

However, once the trial has been completed, any information about you that we collect will have your name and any other identifiable details removed and will be given a special code number. This code number will also be used to identify the questionnaires that you are sent, and the key to the code will be kept in a locked cabinet at the research centre at University College London (UCL) and on a secure computer server. Any identifiable information will be stored separately and securely at the research centre at UCL and locally at the site at which you are recruited (hospital or hospice). Only members of the research team and responsible people authorized by the Sponsor, regulatory authorities or from the NHS Trusts / hospices involved will have access to this data. The Chief Investigator is responsible for the secure archiving of essential trial documents (for each site, if multi-site trial) and the trial database as per their trust policy. All essential documents will be archived for a minimum of 20 years after completion of trial.

Although your GP will be aware that you are taking part in the study, (s)he will not know which treatment you are receiving, (s)he will not have access to any other data you provide as part of the research study (e.g. your answers to the questionnaires).

What happens when the research study stops?

At the end of the nine week visit, your involvement in the study will be finished. At that point you will be treated and monitored in exactly the same way as if you had not been on the study. Your doctor may or may not consider that it is advisable to try using methylphenidate or any other treatment to help with fatigue. This decision will depend upon your current medical condition at that time.

What will happen to the results of the research study?

The study results will be presented at conferences and published in relevant medical journals. None of the people taking part in the study will be identified in reports or publications. If you wish we will send you a brief summary of the results at the end of the study. Copies of any publications can be obtained from the study organisers and sent to any study participants and GPs who wish to have them.

Who is organising and funding the research?

The study is being organised by the Marie Curie Palliative Care Research Department, Division of Psychiatry, University College London. Funding is from the National Institute for Health Research (NIHR) Health Technology Assessment. Some staff working on the project are supported by Marie Curie funding and infrastructure support.

Who has reviewed this study?

This study has been reviewed and approved for its scientific methods by independent researchers in the field appointed by the research funder.

In addition, all research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by London - City & East Research Ethics Committee (REC reference 17/LO/0871).

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions - please see details below.

If you remain unhappy and wish to complain formally, you can do this through your local Clinical Commissioning Group (CCG) Complaints Procedure. Details can be obtained from the relevant CCG. A member of the research team can help you to get these.

Every care will be taken in the course of this study. 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 (University College London) negligence then you may be able to claim compensation.

After discussing this with a member of the research team, please make the claim in writing to Professor Patrick Stone who is the Chief Investigator for the clinical trial and

is based at the Marie Curie Palliative Care Research Department, Division of Psychiatry, University College London. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

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 a member of the research team (details given at the end of this letter) 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 (adverse events) you may have experienced due to your participation in the clinical trial, the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this. Details can also be obtained from the Department of Health website: <http://www.dh.gov.uk>.

What if I have any questions or concerns about the study?

We are providing contact details and telephone numbers and email addresses so you can contact us if you have any questions at any point. We will be happy to ring you back if you wish.

Thank you for taking the time to read this.

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