The ROYAL MARSDEN
NHS Foundation Trust

Drug Development Unit – Information for patients considering participation in a phase I trial

Information for patients

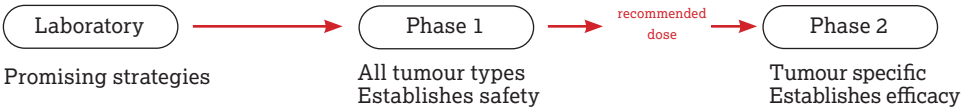
NHS

What does the Drug Development Unit do?

The Drug Development Unit develops and tests new anti-cancer drugs. We do this testing in experimental phase I clinical trials. These are early stage trials of new drugs which are being tested in humans for the first time. Up to this point the drugs would only have been tested in a laboratory. The main aim of a phase 1 trial is to:

- Find out the side effects of a new drug
- Find out the best dose of a new drug
- Understand how the body handles a new drug
- Understand what a new drug does to the body and to the cancer

Phase I trials can also test new combinations of drugs.



How does a phase I trial work?

In a phase I trial, we carefully increase the dose of the drug in small groups of three to six patients with different types of advanced cancer. We start the first group of patients at a carefully selected low dose and monitor them for side effects for at least one cycle (usually three to four weeks). The next group of patients are only given a higher dose of the drug once we know that the previous dose did not cause serious side effects. This process of giving higher doses to different groups of patients continues until we establish a safe and tolerable dose.

Side effects

As this is the first time the new drug is being tested in humans, there is a risk of **unexpected** side effects, and some of these

may be serious. You will be informed of all of the side effects we anticipate from the laboratory studies and what we know from the patients who are already on trial, but some side effects may be unknown. We therefore monitor you closely with weekly visits to the hospital and additional safety tests. We will spend a lot of time discussing possible side effects with you, possibly more time than you have experienced with standard treatments. This is because it is important that you understand the potential side effects and know what to look out for. We can treat most side effects. Sometimes we may need to reduce the dose of the drug and sometimes we may have to stop the trial drug altogether if your health is at risk.

Given the early nature of these trials, we do not know if the drug will benefit any individual patient. Patients referred to our unit would have mostly been given standard treatments for their cancer. Some patients may have a cancer which has no standard treatment options. In this situation, you may want to explore participation in a phase I trial. Information obtained during the course of a phase I trial may contribute to our understanding of cancer and may help us to develop these drugs as future treatments.

Is a phase I trial suitable for me?

Participation in a phase I trial is completely voluntary. Some patients choose not to participate for a number of reasons, which may include:

- Not wanting to have to spend a lot of time in hospital
- Not wanting to risk having side effects from drugs that may not work
- Not feeling well enough.

As safety is the priority for phase I trials, there are strict criteria for participation. This can be disappointing, but a pre-existing medical condition such as hypertension, diabetes, blood clots, heart or eye problems may put you at risk of serious side effects.

Your tests (blood tests, ECGs or scans) may also highlight a reason that would make it unsafe for you to enrol on a phase I trial.

In these situations, you will be discharged back to the care of your referring team. Your GP, palliative care team, and community team will remain involved in your care.

What is the process of getting onto a trial?

First appointment

After being referred by your doctor, you will be seen and assessed in our new patient clinic. This first meeting is important as it is designed to give you lots of information about phase I trials and the opportunity to ask questions.

We realise that this meeting can be overwhelming and we do not expect you to make any immediate decisions about joining a phase I trial. You may wish to take some time to talk to your family, friends or your GP before making a decision. Some people need a repeat appointment to further discuss the issues.

If at this stage you choose not to take part in a phase I trial, or if we think it would not be safe for you to do so, we will ask your doctor to continue with your care.

If after this initial discussion, you would like to take part in a phase I trial and if we think it is safe for you to do so, we will discuss your case at our multi-disciplinary phase I allocation meeting the following week – you should not expect to be offered information on a specific trial at this first appointment.

Allocation

We will review your medical and cancer history, as well as your blood results, scans and ECG prior to discussion at the multi-disciplinary allocation meeting. When allocating a trial for you to take part in, we also take into account your preferences,

your fitness level, and the availability of our trials when making the final decision.

Where possible, we use information about your cancer mutations (genetic drivers of cancer) to help guide decisions about which trial to allocate.

It may therefore take two to three weeks to find you a trial. If we are unable to find a trial for you, we will inform you and your doctor and ask them to continue with your care.

Once we identify a trial for you, we will send you a patient information sheet by post or email. This provides information on the specific phase I trial drug, how it may work, its potential side effects, and how often you need to attend hospital. We will then give you a second appointment to discuss the trial with us in person. Should you decide to take part, you can then sign the consent form in the presence of a doctor at the hospital (not at home). The doctor will also sign the consent form.

Consent

By signing the informed consent form, you confirm that you agree to take part in the trial and that you understand what it will involve. Before signing the consent form you should read the information sheet that you have been given carefully, and discuss all your questions with the doctor. It is very important that you feel you understand all the information you have been given regarding the trial before you sign the consent form.

Screening

Once you have consented, we can start the checking process to ensure that it is safe for you to take part in the trial.
We do this by carrying out some further tests specific to that trial to check your fitness and organ function to ensure that your body could handle the trial drug and any potential side effects.
This screening phase usually involves:

- Blood and urine tests to check organ function
- Physical examination including a check of your blood pressure, heart rate, temperature, breathing rate and oxygen levels to check heart and lung function
- CT or MRI scans to check the status of your cancer
- ECG to check your heart function
- Other specialised tests to check your heart, lung, and eyes.

Some of our phase 1 trials require a biopsy – this will be carefully assessed by our radiologist to check that a biopsy is safe and possible. If you are asked to have a biopsy, you will have an appointment to discuss the details and provide your consent, if you agree.

Once screening is completed, a doctor reviews all of the results. If the results meet the trial safety requirements, plans are then finalised for you to begin the trial.

Why does it sometimes take so long to get onto a trial?

Phase I trials are about being sure that a particular dose of a new drug is safe before we can give a higher dose to other patients. We have to observe patients for a minimum amount of time first before we give the drug to other patients. This means there are necessary breaks between recruiting new patients. All the safety tests and checks have to be analysed and discussed amongst all the trial doctors involved before we can make a decision. Also, a phase I trial usually takes place in anywhere between two and ten hospitals, so we need to coordinate the timings of patients in multiple hospitals and sometimes across different countries.

What happens if my condition changes along the way?

If you become unwell it may not be safe to start the trial. This can be very disappointing but there is a greater chance of serious side effects under these circumstances. Sometimes you might be well, but test results may indicate that it is unsafe for you to take part in the trial. In some cases we are able to suggest another trial where the results of a particular test are not relevant. At other times, the abnormal tests may show that your cancer is growing quickly or that you have another illness that would make participation in experimental trials unsafe.

What does being in the trial involve?

Most trials require that you stay in hospital for the first part of treatment. This can mean being in hospital on our research ward for between one night to five nights. However it is often one or two nights. Some trials may require you to stay in hospital for a second time later in the trial.

While you are in hospital, nurses will take a number of blood samples during the day, usually from a cannula (small plastic tube) in a vein. This blood is taken to a laboratory and tested. We are particularly interested in the levels of the drug in the blood at various times after the drug has been taken. This tells us how your body is handling the drug. You may also be asked to collect urine samples over the day after the drug is given.

After discharge from the hospital, you will be seen at least every week in the clinic to be monitored for any side effects or symptoms from your cancer. Some trials require you to be monitored more closely and so you may need to attend twice a week.

How long do I stay on a trial?

You are free to stop taking part in a trial at any time – before or during a trial – for whatever reason, without your care being affected.

After the first two courses of the trial drug, usually after six to eight weeks, we ask you to have a CT or MRI scan. We compare this to the one taken during screening to see if the drug has had any effect on the growth of your cancer. We also review the side effects you and the other patients on the trial have experienced. If your cancer has stopped growing or shrunk, and if the drug has not given you and other patients too many or serious side effects, you will continue to take another two courses until the next scan. However, if your cancer has got worse, or if you have had serious side effects, then we will stop the trial drug.

For most trials, you continue the trial drug for as long as the scans show that your cancer is not growing and as long as you are tolerating the drug. Some trials set a limit on how many courses you have based on the way the drug being tested may behave.

Sometimes during the course of a trial new information becomes available. Your trial doctor will talk to you about this. We may decide that it is no longer safe for you to continue on this trial and at this point we would stop and consider you for another one. Alternatively, you may be able to continue and we will ask you to sign an updated consent form to do this. Sometimes, patients decide that they no longer want to take part in a trial. If you decide to withdraw from a trial, the doctor will make arrangements for your care to be continued under your referring doctor.

What will my costs be?

A trial is usually sponsored (overseen and managed) by a drug company. The sponsor pays for the medication and the costs of running the trial but does not pay the doctors, nurses or patients

for running the trial or taking part in it. However, you will be paid travel expenses from the day you sign the consent form for the clinical trial.

The costs of any other hospital care that is not part of the trial are met by the National Health Service (NHS). To take part in a trial, patients with private insurance need to switch their care to the NHS.

Who will know about my medical details?

The drug company will have access to your medical history, but this information will have your name and details removed. In this way they would not be able to identify you. All information that the Drug Development Unit collects on you is confidential.

Where can I get more information?

For more information about clinical trials you can read The Royal Marsden patient information booklet *Clinical Trials*. Please ask if you would like a copy. You can also download a copy here:

https://bit.ly/clinicaltrial2

Please take time to read the information you have been given carefully and discuss it with friends or relatives if you wish. Please ask us if there is anything you do not understand or if you would like more information. You can take time to decide whether or not you wish to participate in a trial.

The Drug Development Unit Consultants

Professor Johann de Bono

Professor Udai Banerji

Dr Juanita Lopez

Dr Anna Minchom

If you would like to speak to someone about phase 1 trials then please contact:

The Drug Development Unit Clinical Nurse Specialists (CNS)

Janet Hanwell	020 8642 6011 ext. 1344
Mary Van Zyl	020 8642 6011 ext. 4378
Breda Cooley	020 8642 6011 ext. 1330
Email:	dducns.oak@nhs.net (monitored Monday to Friday)

The Royal Marsden Macmillan Hotline: 020 8915 6899

You can ring the Hotline 24 hours a day, 7 days a week.

Call us straight away if you are feeling unwell or are worried about the side effects of cancer treatments.

This service provides specialist advice and support to all Royal Marsden patients, as well as to their carers, and both hospital and community-based doctors and nurses caring for Royal Marsden patients.

For further information, please visit The Royal Marsden website: *www.royalmarsden.nhs.uk/your-care/support-services/royal-marsden-macmillan-hotline*

Maggie's

Maggie's at The Royal Marsden provides free cancer support and information for people with cancer and their family and friends.

Telephone: 020 3982 3141
Email: maggies.royalmarsden@maggies.org

The centre is located on the corner of Cotswold Road in the grounds of The Royal Marsden, Sutton.

Opening hours: Monday to Friday, 9am – 5pm

References

This booklet is evidence based wherever the appropriate evidence is available, and represents an accumulation of expert opinion and professional interpretation.

Details of the references used in writing this booklet are available on request from:

The Royal Marsden Help Centre

Freephone: 0800 783 7176

Email: patientcentre@rmh.nhs.uk

No conflicts of interest were declared in the production of this booklet.

Should you require information in an alternative format, please contact The Royal Marsden Help Centre.

The patient information service is generously supported by The Royal Marsden Charity.

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Registered Charity No.1095197

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Revised July 2020. Planned review July 2023