Delete this line, then print on Trust/Hospital headed paper

Personalising treatment for myeloma patients based on how well they initially respond to a period of NHS treatment and their overall fitness level

Study registration

We would like to invite you to **join the iFIT research study**

For NHS site reference: standard of care induction DRd 6 cycles

We are a group of doctors, people affected by myeloma, and myeloma researchers. We are from the University of Leeds and around the UK. We have set up this research called iFIT. iFIT is a phase 3 clinical trial of an investigational medicinal product.

We are inviting you to take part because you have myeloma. Your hospital doctor has planned for you to have an NHS treatment called DRd. This is a combination of three medications called daratumumab, lenalidomide and dexamethasone. You usually receive this treatment for as long as it is working, until your myeloma progresses (gets worse).

What will happen if you join? You will have this treatment for around 6 months to start with. After this, we will see how well you have responded and determine your level of fitness. We expect this first 6 months of treatment to pose the same amount of risk as you would have from your usual care. This is because you will be receiving the usual NHS treatment DRd.

What will happen after this? We will give you another document like this one about the further treatment you could receive and check you are willing to continue to take part. The further treatment is personalised based on how well you have responded and your level of fitness. There are some different risks in continuing to take part in the research and receiving the further treatments, compared to your usual care. The further treatment could be:

- Continuing the NHS treatment DRd as long as your myeloma remains under control: This is what you would receive outside of this research therefore the risk is the same.

- Continuing daratumumab and lenalidomide (without dexamethasone). You could receive this for as long as your myeloma remains under control, or stop after 18 28-day cycles:
  Outside of this research you could receive daratumumab and lenalidomide (no dexamethasone). You would usually receive this until your myeloma gets worse. Stopping dexamethasone may mean you have less side effects but could result in your myeloma being less well-controlled. Stopping daratumumab and lenalidomide after 18 cycles will allow you to have a treatment break but could make your myeloma come back sooner.
- Daratumumab plus one of two new immunotherapy treatments (teclistamab or talquetamab) for 18 28-day cycles. Immunotherapy treatments help your own immune system fight myeloma:
  We are using these treatments in a new way in this research. Daratumumab in combination with teclistamab or talquetamab could be more effective in treating your myeloma. There are additional serious side effects associated with these treatments. We will discuss these with if you are planned to have one of these treatments.

As with all research like this, the new treatment may not work as well as the best current treatments. But they might be as good as, or better, than current treatments. We are doing the research because we don't know which is best. Ask your hospital doctor or nurse if you would like to see more details about the risks of the further treatments now.

Throughout the trial, from when you join and after 6 months, we will collect samples of your blood and bone marrow at various times. Sometimes this is just an extra amount to what you are already providing as part of your usual care.

It is completely up to you whether you take part in this research. If you agree to take part, you can change your mind at any time and stop all or some parts of the research. Your usual care won't be affected if you decide not to take part or change your mind later.

How will we use information about you?

In this research study we will use information from you and your medical records. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study.

Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules.

At the end of the study we will save some of the data in case we need to check it and for future research.

We will make sure no-one can work out who you are from the reports we write.

The information pack tells you more about this (See **Appendix 1**).

To help you understand the research, the information is split into several documents:

iFIT document	**This document**	**When will I receive this?**	**What is being asked of me?**
Bone marrow sharing		When having tests to find out if you have myeloma	Do you agree to share a sample of your bone marrow from your planned tests?
Study registration	✓	If you are diagnosed with myeloma	Do you agree to be monitored whilst having the NHS treatment DRd, and for us to collect your data and samples?
Randomised study treatment		After completing a period of the NHS treatment DRd	Do you agree to continue to take part in the research and be randomly allocated to a further treatment based on your data?
Additional information [optional - you don't have to read this before you make your decision]		At the same time as the 'Study registration' document above	Nothing is being asked of you here. This is additional information you may find interesting or helpful.

Ask your hospital doctor or nurse If you would like a copy of any of the above documents. This document has everything you need to know now, but you may want to see what could happen next.

Large-print and electronic versions of all documents are available. Visit https://ctru.leeds.ac.uk/ifit.

Please look through all the information in this '**Study registration**' document before you decide. There is space on page 25 of this document to add questions or notes.

We may update this information during the research. For example, if we learn something new about the treatments. We will tell you about any important updates, and give you the chance to choose if you still want to take part in the research or not.

You will also find some optional extra information in the '**Additional information**' document**.** You don't have to look at this before making your decision, but you may find it useful.

Once you have read the information, your hospital doctor or nurse will talk to you about the research again and you can ask any questions you like.

Contents page

Who can I contact if I have more questions?

If you have any questions about this research, please talk to your **<<enter Consultant, Doctor, Nurse, Researcher>>**:

<< Enter name >>

<< Enter contact details >>

Who is involved in this research?

This research is being run by the Clinical Trials Research Unit (CTRU) at the University of Leeds. The research team includes people affected by **myeloma**.

Your **hospital** is helping us to find people who could take part in this research. They would carry on looking after you during the research, if you take part.

The University of Leeds has overall responsibility for how the research is run.

The research is funded by **Cancer Research UK and Blood Cancer UK, and Johnson & Johnson Innovative Medicine.** Johnson & Johnson Innovative Medicine will provide some of the further treatment drugs used in this research (daratumumab, teclistamab, and talquetamab). The funders are not involved in the day-to-day running of the research. The responsibility for making decisions about the research design and how it is run will always remain with the doctors, statisticians, trial experts, and the people affected by myeloma who are involved.

If I want to, will I definitely be able to take part?

Unfortunately, no. Although your hospital doctor thinks you might be suitable to take part, they will still need to carry out some tests and ask you some questions. They need to make sure you are suitable and that it is safe for you to take part. You may have had some of these tests already and may not need to have them again.

These tests include blood tests, urine tests, bone marrow samples, imaging scans, and pregnancy tests (if you are female and are able to have children).

If your hospital doctor decides the research is not suitable for you, or if you decide not to take part, your hospital doctor will discuss your alternative treatment options with you.

What is the NHS treatment DRd?

Your hospital doctor has planned for you to have treatment with **D**aratumumab, lenalidomide (also known as **R**evlimid®) and **d**examethasone. This is known as DRd. This is an approved treatment for people newly diagnosed with myeloma who are not suitable for a stem cell transplant. DRd treatment is available to patients in the NHS.

Other treatments for newly diagnosed myeloma are available. Talk to your hospital doctor about this.

If you take part in this research, you will receive DRd for around 6 months.

Each treatment cycle lasts 4 weeks (28 days), and you will receive:

- Daratumumab on days 1, 8, 15, and 22 of the first and second cycle, and days 1 and 15 of the third cycle onwards
- Lenalidomide on days 1 - 21
- Dexamethasone on days 1, 8, 15, and 22.

Before the start of each cycle of treatment, your hospital doctor will carry out some tests (including a blood test). This is to make sure it is safe and suitable for you to continue receiving treatment. As long as the tests show you are tolerating and responding to the treatment, you will receive a total of 6 cycles.

Daratumumab is given as an **injection** under the skin, so you may need to come into the hospital on these days. Your hospital doctor will let you know if this is the case. The first time you receive it, you will need to stay to be monitored for a few hours afterwards to check you haven't had a reaction.

Lenalidomide is taken by mouth (orally) as capsules. You can take lenalidomide at home. It is important that you take it exactly as explained by your hospital doctor.

Dexamethasone is taken by mouth as either liquid, soluble or hard tablets. It is important that you take it exactly as explained by your hospital doctor. Dexamethasone may be given as an injection into the vein. Your hospital doctor will advise you if an injection is necessary.

You will also be given some additional medications to help combat the possible side effects of these myeloma treatments. Your hospital doctor will decide exactly which medications you need for this.

What else will happen during the 6 cycles of DRd treatment?

- **Blood and bone marrow samples**

We will collect samples of your blood and bone marrow aspirate (fluid) at the following times:

- Before you start DRd (we will only collect bone marrow aspirate (fluid) if you did not previously share this with us), and
- After you have completed 6 cycles of DRd.

We will take up to an additional 4 teaspoons (20mL) of blood, and 2 teaspoons (10mL) of bone marrow aspirate (fluid) each time.

It is expected that most of the blood samples will be taken at the same time as your routine hospital tests. These should not require any additional needle punctures.

The bone marrow aspirate (fluid) sample after you complete 6 cycles of DRd is not usually performed as part of your usual care. However, the extra sample for this research allows us to personalise your further treatment. Parts of the sample will also be used in laboratory research to understand who responds best to which treatments.

- **Questionnaires**

We will ask you to complete a set of questionnaires at the following times:

- Before you start DRd, and
- After you have completed 6 cycles of DRd.

This is to help us determine the impact of this research on your emotional and physical wellbeing, and how you have used healthcare services.

They can be completed when you attend clinic, or they will be posted to you if you cannot attend. The questionnaires are confidential. Your hospital doctor or nurse will not see what you have written.

- **Data collection**

We will collect further data about you and your health:

- Before you start DRd,
- After 3 cycles of DRd, and
- After you have completed 6 cycles of DRd.

Your hospital doctor will look at some information about you, and if you have any other illnesses. They will also ask you some questions about your lifestyle. This is a way of determining your level of fitness.

We will ask you to complete functional activities, including a short walk test, a memory test and a drawing activity. We will do this to see whether we can find any patterns in how people respond.

What happens after I complete 6 cycles of DRd treatment?

If you decide to continue taking part in the research, your hospital doctor will not decide what further treatment you get after 6 cycles of DRd. Instead, you would get one of the further treatments by chance (randomly). Which treatment you may be allocated to will also be based on:

- How well you have responded to DRd, and
- Your level of fitness.

We allocate treatment randomly so that we can do a fair test of which treatment is best. You should only agree to join the research if you are happy with this.

The further treatments you could receive are:

- Continuing DRd as long as your myeloma remains under control.
- Continuing daratumumab and lenalidomide (without dexamethasone). You could receive this for as long as your myeloma remains under control, or stop after 18 28-day cycles.
- Daratumumab plus one of two new immunotherapy treatments (teclistamab or talquetamab) for 18 28-day cycles. Immunotherapy treatments help your own immune system fight myeloma.

Your myeloma could remain under control for a few months or several years. You will be closely monitored by your hospital doctor for the duration of the research, even if you are no longer having treatment.

We will collect further bone marrow and blood samples, and we will ask you to complete more questionnaires.

There may be reasons why you can't continue in the research and receive the further treatment. However, we would still like to invite you to join the research, as we do not yet know what further treatment you could receive. If you are not able to continue to take part in the research, your hospital doctor will discuss your alternative treatment options with you.

Will I get back any travel or other costs during the research?

You will not receive reimbursement for taking part in this research. This includes:

- Whilst you are receiving DRd treatment, when no additional hospital visits as part of this research are expected.
- If you continue to take part in the research and receive further treatment, when you may need to visit the hospital more often.

What will happen to any samples I give during the research?

The blood and bone marrow samples you give for this research will be split and sent to the iFIT laboratories:

- The Haematological Malignancy Diagnostic Service in Leeds (HMDS) to look at the amount of disease in your bone marrow.
- The Royal Marsden and the Institute of Cancer Research in London (RM/ICR) and the Leeds Institute of Medical Research (LIMR). Researchers there will use the samples to learn about why some people respond better to the treatment than others, or why the disease has progressed (got worse). They will also see if the samples can give a better idea of each person's level of fitness.

We may also share some of your samples with scientists in other research institutes or laboratories in the UK to analyse results for this research.

Some of the iFIT laboratories will extract and/or analyse substances including protein, DNA and RNA from your samples. Researchers there will look to see if any genetic or other patterns can be found in different people and how these relate to several aspects of iFIT research including better understanding frailty, ageing, myeloma and drug response and resistance.

Only the HMDS result taken after 6 cycles of DRd will be shared with your hospital doctor. This is so they can see how well you have responded to DRd. The other results are not relevant to your individual care, so we won't share them.

Your samples will be stored until iFIT is complete, unless you tell us to stop. Your samples will then be kept for future research projects, if you have told us you are happy with that.

Optional parts of the research

- **Use of your samples in future research projects**

The samples which you provide for this research may be valuable in other myeloma research. We will ask if you are willing for your blood and bone marrow samples taken for this research to be used for other myeloma research studies in the future. If you agree to this, we would give access to your samples to other research groups in the UK or abroad.

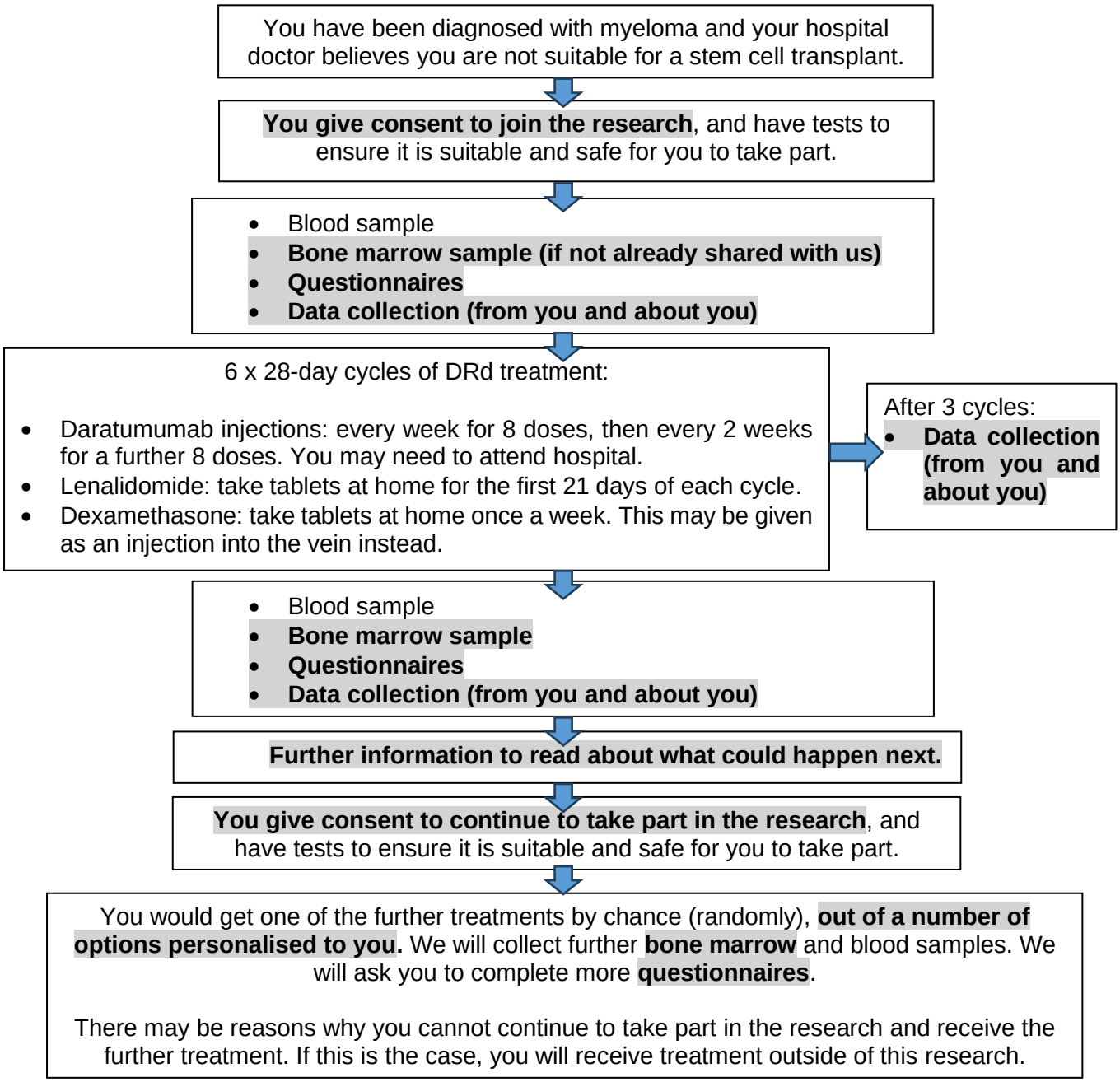
This may be part of a sample which is leftover after doing the tests required for this research. Your samples will be stored in line with good laboratory practices. Data protection regulations will be followed, and strict confidentiality maintained. You will not be identified in the results of any future research. Funding and ethical approval will be obtained for any future research involving your samples.

- **Interviews**

We would like to interview a selection of participants about their experience. There are two separate interviews at different times. We would like your permission to contact you about taking part in these interviews. The interviews are subject to funding and ethical approval. If you agree to be contacted, we will provide further information and see if you would like to take part. We are looking to interview a small number of participants. So even if you are interested in being interviewed, we may not contact you about them.

Summary of information so far

Activities in bold with a grey background will only happen to you if you take part in this research. They would not happen as part of your usual care.



What are the possible benefits of joining this research?

At the end of 6 cycles of DRd treatment, we will look at your individual results to determine your further treatment. This is a form of personalised treatment.

Some of the further treatment options are not available on the NHS. So, you may have access to new treatment combinations. This may or may not be a better approach to treating myeloma compared to the usual approach to treatment in the NHS.

We hope to better understand how the treatments for myeloma compare to each other, and how they are best delivered. Although we can't guarantee you will benefit from taking part in this research, you will help to answer important questions. Answering these questions may improve treatment for people with myeloma now and in the future.

What are the potential risks of joining this research?

DRd is an NHS treatment that you could get in your usual care. So, we do not expect there to be any extra risk to you, compared to your usual care at this point. The potential unwanted effects are listed below.

Completing questionnaires will mean giving up some of your time. Some questionnaires ask about how you are feeling, and this may upset some people, please discuss this with your hospital doctor or nurse. There are links to support pages that you might find helpful in the '**Additional information**' document.

At the end of 6 cycles of DRd, you could receive new treatments that are not used in usual care, and we don't know as much about them yet. So, if you continue to take part, there may be some extra risks compared to your usual care. We will give you further information on the new treatments and ask if you are happy to continue to take part.

Might DRd treatment have any unwanted effects?

All treatments for myeloma have some possible side-effects. There is always a chance of finding out about new side-effects (including potentially serious ones), even in treatments that are commonly used.

If we find out about a serious new side-effect during this research, your hospital doctor or nurse will let you know. They will give you a chance to say if you want to carry on taking part. As the DRd treatment is already used in usual NHS care, it's unlikely we will find out about new side-effects.

You can find a full list of possible side-effects of the DRd treatment on page 18. You should look through these carefully before you agree to take part in this research. Especially if you have concerns about certain side-effects.

Always tell your hospital doctor about any health events you have experienced during your time in the research or afterwards. For example, if you have to go to hospital for any reason. This is to help us protect your safety and the safety of other people with myeloma.

Some of the most potentially common and/or **serious** side-effects are:

- **Injection Site Reactions –** risk with **daratumumab**

Injection site reactions may occur when a treatment is given by injection. Side effects may include but are not limited to:

- Redness
- Itching
- Rash
- Swelling
- Inflammation
- Discomfort
- Bruising
- Hardening of the skin at the site of injection

- **Infusion related reactions –** risk with **daratumumab**

An infusion-related reaction is a reaction that occurs during or after treatment given by injection. It usually occurs during or within the first few hours after the first dose. However, delayed reactions can happen up to 3-4 days after the dose. These reactions can be life-threatening and fatal outcomes have been reported.

Tell your hospital doctor if you:

- Have any respiratory symptoms, such as stuffy nose, cough, throat irritation, chills, vomiting and nausea
- Have a breathing problem or have had breathing problems in the past. This includes chronic obstructive pulmonary disease (COPD) or asthma
- Start to have breathing problems while you are taking part in the research

Most of the reported infusion-related reactions were mild or moderate. The reactions ended by temporarily stopping treatment and/or by taking medications to treat the symptoms. More severe reactions have also been observed that may be life threatening or result in death.

Your hospital doctor will give you medications to reduce the chance of an infusion-related reaction.

- **Anaphylactic and severe skin reactions –** risk with **daratumumab and lenalidomide**

An anaphylactic reaction is a serious allergic reaction that can develop quickly. This could happen within minutes or a few hours, and may cause death.

Let your hospital doctor know if you have any of the following signs or symptoms:

- Itchy rash
- Itchy throat
- Swelling of the tongue
- Shortness of breath
- Vomiting
- Light-headedness
- Low blood pressure

This type of reaction is, for example, seen when someone is allergic to a bee sting or certain foods like peanuts.

- **Infection –** risk with **daratumumab, lenalidomide and dexamethasone**

Daratumumab and lenalidomide may decrease white blood cells. White blood cells help fight infections.

Tell your hospital doctor if you:

- Have an infection or have a history of frequent infections
- Feel sick
- Are diagnosed with COVID-19 or have been in contact with someone with COVID-19

The majority of reported infections have been mild or moderate. Severe infections have been reported and may be life threatening or result in death. Your hospital doctor may give you medications to reduce the risk of severe infection.

Patients who have had prior exposure to the hepatitis B virus are at increased risk of it returning. Your hospital doctor will test you for the hepatitis B virus before you start treatment. If you test positive for the virus, you will be closely monitored for signs of infection. Other viruses that you have been exposed to in the past can also return including cytomegalovirus and herpes zoster virus (shingles).

Dexamethasone can increase the risk of infection, and how severe the infection is. It can also hide the usual signs and symptoms of infections, making them harder to detect.

- **Developing additional types of cancer –** risk with **lenalidomide**

People having treatment for myeloma may develop second cancers. This risk may increase with lenalidomide. Most of the cancers reported are skin cancers that can be easily manged. However, other serious second cancers have been reported including blood cancers such as:

- Acute myeloid leukaemia
- Myelodysplastic syndrome

Your hospital doctor will look at the benefit and risk with you.

- **Developing a blood clot** – risk with **lenalidomide**

Myeloma increases the risk of developing a blood clot. This risk is further increased with lenalidomide. Your doctor will give you a medication to reduce the risk of developing one. Blood clots most commonly occur in the legs and lungs. Symptoms of a leg clot include swelling or pain in one of your legs. Symptoms of a lung clot include shortness of breath or pain on taking a deep breath in. If you experience any of these symptoms let your hospital doctor know.

Do I need to use contraception during this research?

The treatment in this research is potentially harmful to unborn children. If you are pregnant, think you may be pregnant, or are planning to become pregnant, then you cannot take part in this research.

If you join the research and are able to have children you must use at least one effective method of contraception for at least 4 weeks before starting treatment, during treatment, and until at least 3 months after finishing treatment (up to 5 months after stopping teclistamab treatment). This must be continued even if you have a break from treatment. Your doctor will discuss with you what methods of contraception are considered to be effective. Alternatively, you can commit to absolute and continuous abstinence from sexual intercourse and will be asked to confirm this on a monthly basis. You will also need to have a medically supervised pregnancy test when joining the research and every 4 weeks before starting each cycle of daratumumab, lenalidomide and dexamethasone treatment. Female participants who are able to have children may also need to have pregnancy tests before starting each cycle of teclistamab or talquetamab treatment.

If you join the research and are the male partner of a woman who is pregnant or is able to have children who is not using effective contraception, you must use contraception from the time of signing the consent form up to 7 days after stopping lenalidomide treatment (up to 3 months after stopping teclistamab treatment). This applies even if you have had a vasectomy.

Blood and semen or sperm donation is not allowed whilst receiving treatment and for 7 days after completing lenalidomide treatment.

If you or your partner do become pregnant during your participation in the research, we will need to collect some basic information about the mother and child, and their health. The information we collect will not identify the mother (if it isn't you) or child. We will use this information to see how the mother and child are doing.

Inform your hospital doctor if you become pregnant and stop study treatment immediately. If you are a male participant and your partner becomes pregnant, please report it immediately.

Will I be exposed to radiation if I take part in this research?

You may have a bone imaging scan when you join the research. If you have had a scan within the 14 weeks prior, you will not need to have another when you join. The scan may be a whole body low dose CT, PET CT scan, MRI scan or other investigations, depending on what your hospital normally uses. This is to form images of your body and provide your doctor with information about your myeloma. Scans with a “CT” portion involve exposure to ionising radiation, MRI scans do not. Further scans may be performed throughout the research if your hospital doctor feels these are required to monitor your disease. However, these will only be done if necessary, and would be done even if you were not taking part in this research.

If you take part in this research, you will have imaging of your bones which may be CT or PET CT or MRI. Some of these will be extra to those that you would have if you did not take part. The CT and PET CT procedures use ionising radiation to form images of your body. Ionising radiation may cause cancer many years or decades after the exposure. The chances of this happening to you as a consequence of taking part in this study is about 0.5%.

What else should I be aware of during this research?

Some people with myeloma find that they can **continue to work during treatment**, but this might not be the case for all. Your hospital doctor will be able to provide you with detailed advice about your treatment and how it may affect you.

During the initial few months of treatment, **holidays abroad may be difficult**, but short breaks are possible. Discuss this with your hospital doctor.

Complementary health supplements such as St John’s Wort, as well as some medications, should not be used during this research as they may interact with the treatment. **Let your hospital doctor know if you are taking any medications or complementary health supplements**.

You must not receive any live vaccinations 30 days before joining the research and for 3 months after you have completed all treatment. Examples of common ‘live’ vaccines include the chicken pox, yellow fever, shingles (Zostavax), and the measles, mumps and rubella (MMR) vaccines. **Check all vaccinations with your hospital doctor**.

Tell your health care providers that you are taking daratumumab **before receiving a blood transfusion**.

You should take care that your **tablets are kept in a safe place** and **in line with any instructions** given for storage. Any unused tablets should be returned to the hospital pharmacy. You will be asked to complete a diary to record when you take the medication correctly, or if you forget or

take an incorrect amount of mediation. **Let your hospital doctor know if you have not taken the medication correctly**. There is space in the diary for you to list any side-effects you have.

You will be given a **daratumumab card** that you should carry with you at all times.

What if the treatment in this research doesn't help?

If the treatment is not working and your myeloma progresses (gets worse), your hospital doctor will discuss other options with you. Decisions regarding treatment will be always made in your best interest.

How is the research checked while it's happening?

A group of doctors and statisticians who are not linked to the research team will check the progress of the research regularly. They will recommend that the research stops for all participants if they see that it is no longer safe, or that one of the treatments is clearly better than the other.

What if I become unable to make my own decisions during the research?

It is expected to be very rare that you would lose mental capacity during this research. However, this could happen to anybody (e.g., if someone had a head injury).

If this did happen to you, you would continue with the treatment in this research if your hospital doctor and your family or carer thought it best for you to do so. We would continue to collect information about you as part of this research.

What will happen to me after I finish all study treatment?

After you have received 6 cycles of DRd treatment and further treatment, your hospital doctor will discuss and agree with you any more treatment you may need.

What will happen to the results of the research?

When the research is complete, the results will be published in a medical journal and on UK cancer organisation websites such as Myeloma UK, Cancer Research UK, and Blood Cancer UK.

Results of research projects are often presented at large medical meetings to make sure as many doctors as possible know about the results. This is how research can improve treatment and care.

We will make sure you have a chance to find out the results of the research, if you would like them. You will still be able to have a copy of the research results if you stop taking part before the end.

No individual participants will be identified in the results.

Research like this can take a while to complete. The results might not be ready for a number of years. You can stay in touch with our progress here: https://ctru.leeds.ac.uk/ifit. We expect to collect information for this research until 2036.

What if something goes wrong during the research?

If a medical emergency related to your treatment for this research occurs while you are at home, you should contact the hospital where you received your treatment or you should go to the Accident and Emergency (A&E) department of your local hospital.

If you are unable to get to the hospital you should contact your GP who will already have been informed that you are taking part in this research.

What if I am harmed by taking part in this research?

Every care will be taken in the course of this research. However, in the unlikely event that you are injured as a result of the managing organisation (University of Leeds), compensation may be available, and you may have to pay your related legal costs.

Your hospital where you receive your treatment has a duty of care to you whether or not you agree to participate in the research and the University of Leeds accepts no liability for negligence on the part of your hospital's employees.

If you wish to complain about any aspect of the way you have been treated, please contact your hospital doctor or nurse in the first instance.

Any claims will be subject to UK law and must be brought in the UK.

If you have private medical insurance, you should tell your insurer that you are taking part in research. They will let you know if it affects your policy.

Full details of potential treatment side effects

The frequency of side-effects is usually described as **very common** (seen in at least 1 of every 10 patients), **common** (seen it at least 1 of every 100 patients), **uncommon** (seen in at least 1 of every 1,000 patients), **rare** (seen in at least 1 of every 10,000 patients). The severity of side effects can vary but some may be life-threatening or result in death.

Side-effects in **bold** below are further described in the risks and unwanted effects section above.

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
Infections	Infection of the upper respiratory tract such as nose, sinuses, throat, or upper airway	Very common	Very common	
	Infection of the lower airway (bronchitis) and lungs (pneumonia)	Very common	Very common	
	Urinary tract infection	Common	Common	
	Flu-like symptoms (including fever, cough, muscle aches/pain, headache, and chills)	Common	Very common	
	Sepsis (a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs)	Common	Common	
	COVID-19	Very common		
	Cytomegalovirus infection	Uncommon		
	Liver infection (hepatitis) in those patients who are carriers of the hepatitis B virus	Uncommon	Uncommon	
	Cellulitis (bacterial skin infection that causes redness, swelling, and pain in the infected area of the skin)		Common	
	Gastrointestinal tract infection		Common	
	Recurrence of dormant tuberculosis (an infection that mainly affects the lungs but can affect other parts of the body like the brain, kidneys, or spine)			Uncommon
	Decreased responsiveness to vaccination and skin tests	Common	Common	Common
	Other bacteria, viral, and fungal infections (including infections from organisms that wouldn’t normally cause	Very common	Very common	Common

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
	infection in healthy individuals) that could affect any body site			
	Increased risk of infections, with masking of symptoms and signs that this is occurring			Common
Cancerous and non-cancerous growths of tissue (including cysts, a growth usually filled with fluid, and polyps, small clumps of cells that form on the lining of organs)	Skin cancers including basal cell carcinoma, squamous cell carcinoma		Common	
	Haematological malignancies including acute myeloid leukaemia, myelodysplastic syndrome, and T-cell type acute leukaemia		Common	
	Breakdown of tumour cells leading to harm to kidneys and other organs		Uncommon	Uncommon
Blood and the lymphatic system (part of the body's immune system)	Low white blood cells (including neutropenia, lymphopenia, leukopenia); may increase the risk of getting an infection	Very common	Very common	
	Increased white blood cells			Common
	Low platelets (thrombocytopenia); may increase the risk of bleeding and bruising	Very common	Very common	
	Low red blood cells (anaemia), due to decreased production or increased breakdown or loss by bleeding	Very common	Very common	
	Bleeding		Very common	
	Fever with low white blood cells (febrile neutropenia)		Common	
	Problems with blood clotting		Common	
The immune system	**Anaphylactic reaction**	Rare	Rare	Rare
	Hypogammaglobulinemia, a condition of your immune system in which not enough gamma globulin proteins (also known as antibodies) are produced. Decreases in gamma globulin proteins can increase the risk of infections	Common		
	Hypersensitivity (an overreaction of the immune system to something that is usually harmless)		Uncommon	Rare
How the body uses food, produces important chemicals, and gets the nutrients it needs to stay healthy	Loss of appetite and weight loss	Very common	Very common	
	High blood glucose levels (hyperglycaemia)	Common	Very common	
	Low blood calcium levels (hypocalcaemia)	Common	Very common	Common

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
	Loss of body fluids, also known as dehydration	Common	Very common	
	Low blood potassium levels (hypokalaemia)		Very common	Common
	Low levels of sugar in the blood (hypoglycaemia)		Very common	
	Low blood sodium levels (hyponatraemia)		Very common	
	Low blood magnesium levels (hypomagnesaemia)		Common	
	High blood urea levels (hyperuricaemia)		Common	
	High blood calcium levels (hypercalcaemia)		Common	
	Increased blood sugar levels, diabetes mellitus, or worsening of blood sugar control in those already with diabetes mellitus		Common	Common
	Low blood phosphate levels (hypophosphataemia)		Common	
	Swelling and pain in small joints (gout)		Common	
	Suppression of the “stress response” axis (hypothalamic-pituitary-adrenal axis) which may impair response to stressors such as trauma, surgery, inflammation, and infection			Very common
	Rounding of face shape			Common
	Increased body hair growth			Common
	Increased appetite and weight gain			Very common
	When the thyroid gland in the neck isn't producing enough hormones needed to regulate the body's energy levels (hypothyroidism)		Common	
	Fatigue or lack of energy	Very common	Very common	Common
The brain and how we think and behave	Sleeplessness (insomnia)	Very common	Very common	Very common
	Depression		Very common	
	Loss of sex drive		Uncommon	
	Affective disorders (such as irritable, euphoric, depressed, and labile mood and suicidal thoughts)			Common
	Psychotic reactions (including mania, delusions, hallucinations, and aggravation of schizophrenia)			Common
	Behavioural disturbances			Very common
	Irritability			Very common

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
	Anxiety			Common
	Sleep disturbances and difficulty “thinking straight” including confusion and forgetfulness			Very common
The nervous system	Abnormal sensation including numbness/tingling of hands, feet, or limbs (sensory neuropathy, paresthesia)	Very common	Very common	
	Headache	Very common	Very common	
	Dizziness	Common	Very common	
	Fainting	Common	Common	
	Tremor or shaking of hands of feet		Very common	
	Altered sense of taste		Very common	
	Difficulty maintaining balance (balance impaired) and fall		Common	
	Pain from nerve damage		Common	
	Altered sense of touch		Common	
	Stroke or mini stroke (transient ischaemic attack		Common	
	Bleeding in the brain		Uncommon	
The eyes	Cataracts		Very common	Very common
	Blurred vision		Very common	Common
	Reduced clarity in vision (reduced visual acuity) – a need for glasses/lenses identified on opticians/optometry test		Common	Common
	Blindness		Uncommon	Uncommon
	Increased pressure inside the eye (increased intra-ocular pressure) or glaucoma			Common
	Swelling of the nerve responsible for vision			Uncommon
	Posterior subcapsular cataracts - a type of cataract that forms in the back of the lens and can significantly impact vision			Uncommon
	Thinning of aspects of the eye			Uncommon
	Worsening of eye infections			Uncommon
	Fluid build-up at the back of the eye (chorioretinopathy)			Uncommon
The ears	Loss of hearing		Common	
	Ringing in the ears (tinnitus)		Common	
The heart	Irregular heartbeat (atrial fibrillation) or fast heart rate	Common	Common	

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
	Slow heart rate		Common	
	Changes to the heart rhythm (arrhythmia, QT prolongation, atrial flutter, ventricular extrasystoles)		Uncommon	
	Heart attack (myocardial infarction or ischaemia) (including acute)		Common	
	Heart failure		Common	
	A tear in the heart muscle after a recent heart attack (myocardial rupture following recent myocardial infarction)			Common (in the case of recent heart attack)
The blood vessels	High blood pressure (hypertension)	Common	Common	Common
	Bloods clots in the veins or arteries (predominantly deep vein thrombosis and pulmonary embolism)		Very common	Common
	Low blood pressure (hypotension)		Very common	
	Bruising		Common	Common
	Inflamed blood vessels (vasculitis)		Common	
	Ischemia, including peripheral ischaemia		Uncommon	
	Blood clots in the veins of the brain (intracranial venous sinus thrombosis)		Uncommon	
The lungs and airways	Cough	Very common	Very common	
	Shortness of breath (dyspnoea), including wheezing	Very common	Very common	
	Fluid in the lungs (pulmonary oedema)	Common		
	Nose bleeds		Very common	
	Altered voice quality		Common	
	Difficulty breathing		Common	
	Chest pain		Common	
	Low oxygen level (hypoxia)		Common	
	Hiccups			Common
The digestive system, including the stomach, intestines and any other part of the body involved in digesting food and absorbing nutrients	Diarrhoea	Very common	Very common	
	Constipation	Very common	Very common	
	Nausea / vomiting	Very common	Very common	Common
	Inflammation of the pancreas gland (pancreatitis)	Common		Uncommon
	Stomach pain		Very common	

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
	Indigestion (dyspepsia)		Very common	Common
	Dry mouth		Very common	
	Mouth swelling (stomatitis)		Very common	
	Bleeding from the gastrointestinal tract (including mouth, stomach, intestine and rectum/anus)		Common	Common
	Trouble swallowing (dysphagia)		Common	
	Inflammation of the large intestine		Uncommon	
	Blockage of the bowel		Common	
	Stomach ulcer (peptic ulceration) that may be severe with a tear and bleeding from the stomach			Uncommon
	Gullet ulcers (oesophageal ulceration) and fungal infection (candidiasis)			Uncommon
The liver, gallbladder and bile ducts	Abnormal liver blood tests		Very common	
	Liver injury/damage		Common	
	Liver failure		Uncommon	
	Gallstones		Common	
The skin and the layer of tissue just beneath it	Rash, a noticeable change in the texture or colour of the skin	Very common	Very common	
	Itchy skin (pruritus) or eczema	Common	Very common	
	Hives (urticaria, redness in lumps) or erythema (redness all over the skin)		Common	
	Excessive sweating		Common	
	Dry skin		Common	
	Increased pigmentation of skin usually presenting as darker skin in some areas.		Common	
	Severe reaction called DRESS syndrome (drug rash with eosinophilia and systemic symptoms) which usually presents as a skin rash but can also lead to damage to internal organs.		Uncommon	
	Skin discolouration		Uncommon	
	Increased sensitivity of the skin to sunlight		Uncommon	
	Increased time for the skin to heal (impaired skin healing)			Common

Side effect group	Side effect	Related to **daratumumab**	Related to **lenalidomide**	Related to **dexamethasone**
	Thinning of the skin			Common
	Bruising		Common	Common
	Skin marks including as lines (striae) or threadlike/wider veins (telangiectasia)			Common
	Acne			Common
The muscles, bones, joints and tissues that connect different parts of the body	Muscular pain in the chest	Common		
	Weak muscles, particularly of big muscles like thighs and upper arms		Very common	Common
	Pain in bones		Very common	
	Muscle pains or spasms (including back pain)	Very common	Very common	
	Joint pain or swelling	Very common	Very common	
	Fragile bones (osteoporosis)			Very common
	Bone fractures			Common
	Loss of blood supply to bones (avascular osteonecrosis)			Common
	Break of tendon (tissue that holds muscle to bone together)			Common
	Swelling of face, hands, feet, or limbs (oedema peripheral)	Very common	Very common	Common
	Lack of strength (asthenia)	Very common	Very common	
The kidneys and urinary tract	Kidney failure		Very common	
	Blood in urine		Common	
	Loss of control of urination or inability to pass urine		Common	
	Other types of kidney damage (e.g., acquired Fanconi syndrome, renal tubular necrosis)		Uncommon	
The reproductive system	Erectile dysfunction		Common	
	Irregular or stopped periods/menstruation			Common
Other	**Injection site reaction:** local reaction reported as mild pain or a burning sensation at the site of injection in the abdominal wall. Redness and hardening of the skin at the injection site was also observed and usually disappeared within a few hours after the administration	Common		
	Infusion-related reactions	Unknown		

Any questions?

You can use this space to write down any questions/notes you have about the research. You can then share them with your hospital doctor or nurse.

Space for questions/notes

Appendix 1

How will we use information about you?

We will need to use information from you and from your medical records for this research project.

This information will include your:

- Identifiable information, such as your full name, NHS number (or CHI number for Scotland), and date of birth.
- Full postcode. This is so we can make sure a range of different people are included in our research.
- Email address and/or mobile phone number, for contacting you to complete and reminding you to complete questionnaires online. This will be collected after 6 cycles of DRd treatment. We will only collect these if you choose to complete questionnaires online.
- Results from your medical tests, when they are relevant to the research.
- Results from samples analysed at the laboratory at your hospital, to look for certain genetic abnormalities.
- Results from the analysis of your samples sent to the iFIT laboratories (such as HMDS, LIMR, and RM/ICR).
- Imaging and results or reports from imaging, scans, or other investigations, for central review. This includes any bone imaging scans taken in the 14 weeks prior to joining the research.

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 will have a code number instead.

The University of Leeds is the sponsor of this research.

The University of Leeds is responsible for looking after your information. We will share your information related to this research project with the following types of organisations:

- Laboratories. Your samples will be sent to the iFIT laboratories alongside information about you such as NHS number (or CHI number for Scotland), date of birth, sex and initials. Your samples sent to HMDS in Leeds will also include your full name. This helps ensure your samples are correctly identified as yours.
- The pharmaceutical company Johnson & Johnson Innovative Medicine.
- Regulatory bodies.

- NHS England or other central UK NHS bodies.
- Your GP Surgery (only about your taking part).
- Other organisations with trusted researchers who are working on research in the public interest. We will only do this for worthwhile research projects with all appropriate approvals.

We will keep all information about you safe and secure by:

- Carefully planning how we will collect and use your information, so that we know it will be done securely.
- Only using information that will identify you when we really need to.
- Holding information in very secure databases so that it would be very difficult for unauthorised people to access it.
- Storing any paper documents in locked cabinets, accessible only to people who need access to run the research.
- Training all our staff on how to use people's information correctly.

International transfers

We may share or provide access to data about you outside the UK for research related purposes to:

- Allow Johnson & Johnson Innovative Medicine, an international pharmaceutical company involved in this research, to learn more about the effects of some of the research treatments.
- Share the information we collect in this research study for other research projects.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- The pharmaceutical company Johnson & Johnson Innovative Medicine, an international company involved in this research.
- Other organisations with trusted researchers who are working on research in the public interest. We will only do this for worthwhile research projects with all appropriate approvals.

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- We do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says.
- We need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing.
- We have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when this is legally required. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/report-a-breach.

How will we use information about you after the study ends?

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.

We will keep your study data for the minimum period of time required by laws and other rules about research. These say it must be possible to check the results of the research study for a period of time after it has finished. This means we will need to keep your identifiable information until at least 25 years after the research study has finished. The study data will then be fully anonymised and securely archived or destroyed.

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.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records and your hospital. If you do not want this to happen, tell us and we will stop.
- You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

- 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, including the specific mechanism used by us when transferring your personal data out of the UK:

- Our leaflet https://ctru.leeds.ac.uk/privacy-cookies/how-we-use-personal-data/ and www.hra.nhs.uk/patientdataandresearch
- By asking one of the research team
- By sending an email to DPO@leeds.ac.uk, or
- By ringing us on +44 (0)113 343 7641.

Delete this line, then print on Trust/Hospital headed paper

CANCER RESEARCH UK | ctru University of Leeds | LEEDS CLINICAL TRIALS UNIT | Blood cancer UK

Participant ID:	Initials:
Date of Birth:	NHS number (or CHI number for Scotland):
ISRCTN:	Principal Investigator:

PARTICIPANT INFORMED CONSENT DOCUMENT FOR STUDY REGISTRATION

Please initial for each statement

1. I confirm that I have read through the study information document and have had the opportunity to ask questions. _ _ _ _ Initials

2. I understand that my participation in this research is voluntary and that I am free to withdraw at any time without my medical care or legal rights being affected. I understand that even if I withdraw from the above research, the data and samples collected from me will be used in analysing the results of the research, and in some cases, further information about any unwanted effects of my treatment may need to be collected by the research team. _ _ _ _ Initials

3. I understand that my healthcare records may be looked at by authorised individuals from the research team, the University of Leeds, regulatory bodies, or Johnson & Johnson Innovative Medicine to check that the research is being carried out correctly. _ _ _ _ Initials

4. I understand that some of my data may be passed to other organisations, such as the pharmaceutical company Johnson & Johnson Innovative _ _ _ _ Initials

Medicine. This is to monitor the safety of the treatment(s) that I am receiving. I understand that my identity will remain anonymous.

5. I agree to blood and bone marrow samples being collected, stored, and used for research investigations that form part of the iFIT (UK-MRA Myeloma XVIII) research, and understand that this will include genetic research. I understand that the samples will be sent along with information about me, which will include NHS number (or CHI number for Scotland), and may include my name. _ _ _ _ Initials

6. I understand that results of my medical tests and other data may be shared with other research teams if I am taking part in another research project run by the University of Leeds. _ _ _ _ Initials

7. I agree that information collected about me in this research can be shared with researchers outside the original team, so they can do additional research projects. This could include researchers outside the UK. Researchers outside the original team would not be able to identify me from the information they get. _ _ _ _ Initials

8. I agree for my details (which will include my name, date of birth, and NHS number (or CHI number for Scotland)) to be submitted to NHS England or other central UK NHS bodies so that information about my health and mortality, should this become available, may be obtained by the CTRU. _ _ _ _ Initials

9. I agree to a copy of this Consent Form being securely sent to the Leeds Clinical Trials Research Unit. I understand that this will show my name and signature. _ _ _ _ Initials

10. I agree that my GP, or any other doctor treating me, can be notified of my participation in this research. _ _ _ _ Initials

11. I agree to take part in the iFIT research. _ _ _ _ Initials

The following points are OPTIONAL.

Even if you agree to take part in this research, you do not have to agree to this section.

	Please initial 'Yes' or 'No'	
12. I agree to be contacted by the research team with further information about the participant experience interviews.	**YES**	**NO**
	_ _ _ _ Initials	_ _ _ _ Initials
13. I agree for my blood and bone marrow samples to be used in future research that receives ethical approval. I understand that my samples and information collected from it may be shared with	**YES**	**NO**
	_ _ _ _ Initials	_ _ _ _ Initials

researchers in the UK and potentially outside the UK. I understand that these researchers will not be able to identify me.

We would like to know your ethnicity, sex, and gender to help us further understand the diversity of our participant population and improve the accessibility of our trials to as wide a group of people as possible in the future. This information will be treated as confidential and will not affect your entry into the study or your care.

14. I agree to provide my ethnicity **YES** **NO**

_ _ _ _ Initials _ _ _ _ Initials

If yes, please provide your ethnicity by ticking **or** writing below:

Asian or Asian British

☐ Indian
☐ Pakistani
☐ Bangladeshi
☐ Chinese
☐ Any other Asian background

Black, Black British, Caribbean, or African

☐ Caribbean
☐ African
☐ Any other Black, Black British, or Caribbean background

Mixed or multiple ethnic groups

☐ White and Black Caribbean
☐ White and Black African
☐ White and Asian
☐ Any other Mixed or multiple ethnic background

White

☐ English, Welsh, Scottish, Northern Irish, or British
☐ Irish
☐ Gypsy or Irish Traveller
☐ Roma
☐ Any other White background

Other ethnic group

☐ Arab
☐ Any other ethnic group

<u>Or</u>, if you would prefer to describe your ethnicity yourself, please write in the box below

15. I agree to provide my sex and gender **YES** **NO**

_ _ _ _ Initials _ _ _ _ Initials

If yes, please provide your sex assigned at birth in the box below:

If yes, please provide your gender identity in the box below:

Patient (to be completed by the patient):

Signature……

Name (block capitals)……

Date……

Investigator:

I have explained the research to the above-named patient and they have indicated their willingness to participate.

Signature……

Name (block capitals)……

Date……

We would like to compare the formal level of fitness assessment with your clinical opinion. Please provide your clinical opinion of the patient's level of fitness by ticking one of the boxes on the next page **before** calculating the IMWG frailty score.

Witness:

I have completed this consent form on behalf of the person named above who has freely given their consent to participate.

Signature……

Name (block capitals)……

Date……

(1 copy for patient; 1 for the CTRU; 1 held in patient notes; original stored in Investigator Site File)

This page is for investigator completion only and is not to be given to the participant

We would like to compare the formal level of fitness assessment with your clinical opinion. Please provide your clinical opinion of the patient's level of fitness by ticking one of the boxes below **before** calculating the IMWG frailty score:

☐ FIT ☐ UNFIT ☐ FRAIL

Investigator (the same investigator who performed consent):

Signature……

Name (block capitals)……

Date……