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

Randomised study treatment

We would like to invite you to **continue to take part in iFIT and receive further treatment**

*For NHS site reference: **iFIT2** (MRD+ and FRAIL) – DRd until PD / DR until PD*

Thank you for taking part in iFIT so far. You have now completed 6 cycles of the NHS treatment DRd (daratumumab, lenalidomide and dexamethasone).

This information explains the further treatment you could receive, based on your recent tests. The tests show that you have current detectable myeloma cells in your bone marrow (MRD positive), and that you have a lower level of fitness (frail category).

We will test if stopping the dexamethasone part of DRd treatment would allow people to continue the treatment for

longer, with fewer side effects and without making their myeloma worse.

It is completely up to you whether you continue to take part in this research. Your usual care won't be affected if you decide not to continue.

There are some different risks in continuing to take part in the research, compared with your usual care. Discuss the possible risks with your hospital doctor.

If you agree to take part, you can change your mind at any time and stop all or some parts of the research. If you want to change your level of involvement, just let your hospital doctor or nurse know.

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** in the **'Study Registration'** document).

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?

iFIT document	This document	When will I receive this?	What is being asked of me?
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.

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

Ask your hospital doctor or nurse if you need another paper copy of the '**Study registration**' or '**Additional information**' documents. You were given a copy of these when you joined

the research. These contain information that is still applicable to you now.

Please look through all the information in this '**Randomised study treatment**' document before you decide whether you would like to continue. There is space on page 15 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 or not.

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 >>

Can I receive any of the other further treatments?

Unfortunately, no. You are only able to receive one of the further treatments described in this document. These further treatments are based on your response to the NHS treatment DRd and your level of fitness. Neither you nor your hospital doctor can change this.

You do not have to continue to take part in this research if you do not want to.

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

Unfortunately, no. Although you will be allocated one of these further treatments based on your initial response and fitness, your hospital doctor 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 further treatment could I receive?

If you decide to continue to take part in this research, your hospital doctor will not decide what treatment you get out of the options listed here. Instead, you would get one of the treatments by chance (randomly).

This means if you agree to continue to take part, you will have an equal chance of getting either of the treatments. You should only agree to continue to take part if you are happy with this.

We do this so that we can do a fair test of which treatment is best. We only do this because we do not know which of the treatments is best.

This process is called randomisation, and you will be randomised to one of the following treatments:

1. **Continuing Daratumumab, lenalidomide (also known as Revlimid®) and dexamethasone (DRd therapy) as long as your myeloma remains under control.** This could be a few months or several years.

   This is continuing the NHS treatment that you would likely receive even if you were not taking part in this research.

   You will continue your treatment as you have been. However, the daratumumab **injection** will be reduced to once a month (on day 1 of each 28-day cycle).

OR

2. **Continuing Daratumumab and lenalidomide (also known as Revlimid®) as long as your myeloma remains under control.** This could be a few months or several years.

   You will continue your treatment as you have been. However, the daratumumab **injection** will be reduced to once a month (on day 1 of each 28-day cycle), and you will no longer take dexamethasone.

Before the start of each cycle of treatment, your hospital doctor will carry out some tests (including a blood test) to make sure it is safe and suitable for you to continue receiving treatment. You will continue to receive the treatment as planned, if the tests show you are tolerating the treatment, and your myeloma remains under control.

Other treatments are available. Talk to your hospital doctor about this.

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

Occasionally on receiving new information, your hospital doctor may consider it be in your best interest that you stop taking any further study treatment.

What else will happen?

- **Blood and bone marrow samples**

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

- After 6 cycles of treatment (blood only), and
- If you are no longer responding to treatment.

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.

You would likely have a bone marrow sample taken if you are no longer responding to treatment, even if you were not taking part in this research.

- **Questionnaires**

We will ask you to complete a total of 6 further sets of questionnaires. This will be at 3, 6, 12, 18, 24 and 30 months from randomisation (when you are allocated by chance to a further treatment). If you stop treatment, we will still ask you to complete these around the time they would have been due.

This is to help us determine the impact of this research on your emotional and physical wellbeing, and how you have used healthcare services. The questionnaires are confidential. Your hospital doctor or nurse will not see what you have written.

You may continue to complete the questionnaires on paper, or you may now change to completing the questionnaires online.

If you choose to complete the questionnaires online, we will collect your email address and/or mobile number, and you will be sent a link to complete by the method you prefer. You will receive up to 3 reminders to complete each questionnaire.

Please let your hospital doctor or nurse know if you change your email address or phone number during the research. Otherwise, we might not be able to send questionnaires to you in this way.

A guide to completing your questionnaires using the online method is provided in the '**Additional information**' document.

- **Data collection**

We will collect further data about you and your health.

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. This will happen after every 6 cycles of treatment for a maximum of 6 times.

Why are you investigating stopping dexamethasone treatment?

Dexamethasone is associated with some unpleasant side effects, particularly for people with myeloma with a lower level of fitness.

We do not know whether stopping dexamethasone is better when you have current detectable myeloma cells in your bone marrow.

We will look at if stopping dexamethasone would allow people to continue on the treatment for longer, with fewer side effects, and without making their myeloma worse.

Even if you decide not to continue to take part in iFIT, it is possible that your treatment may involve stopping dexamethasone.

What are the possible benefits of continuing to take part?

People with myeloma who have previously received the NHS treatment DRd have often asked if dexamethasone can be stopped safely.

By continuing to take part, you will help us answer this important question, even if you are not randomised (by chance) to stop dexamethasone treatment.

We are doing this research because we do not know whether it is best to stop dexamethasone at this stage or not. We want to find out which is best at the end of the research. It might be that the treatment option you get in the research is better, but we won't know until the end of the research.

What are the potential risks of stopping dexamethasone?

We do not know whether stopping dexamethasone will benefit you or if it may result in your myeloma being less well controlled.

What are the potential risks and unwanted effects of daratumumab, lenalidomide and dexamethasone?

Refer to the '**Study registration'** document for risks and side effects associated with daratumumab, lenalidomide and dexamethasone, as well as other information we want to make you aware of. Talk to your hospital doctor or nurse if you need another copy of the '**Study registration**' document.

If you are randomised (by chance) to receive daratumumab and lenalidomide (without dexamethasone), the dexamethasone side effects will not be applicable to you.

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

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

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

PARTICIPANT INFORMED CONSENT DOCUMENT FOR RANDOMISATION (iFIT2)

Please initial for each statement

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

_ _ _ _
Initials

2. 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

3. I agree to continue my participation in the research and receive one of the further treatments by chance (randomly). _ _ _ _ Initials

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……

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)