

# Myeloma XII (ACCoRd)

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**This Infosheet provides information about what the Myeloma XII clinical trial is, why it is taking place and what is involved if patients decide to take part in the trial.**

This Infosheet does not replace the information about the trial that the hospital will provide to any patients considering taking part. This will be more detailed. Patients considering taking part in the Myeloma XII trial but who have not received information about it from the hospital should speak to their doctor. Bold terms are explained in a glossary at the end of the Infosheet.

## **What is the Myeloma XII clinical trial?**

The Myeloma XII trial, also known as the ACCoRd trial, is a Phase III clinical trial. Phase III trials are carried out in large groups of patients to confirm the effectiveness of a new treatment, compare it to other commonly used treatments, monitor side-effects and collect information that will allow the new treatment to be used safely.

Myeloma XII is one of the latest in a series of national myeloma trials developed by the National Cancer Research Institute. These trials have been responsible for some notable discoveries that have improved the understanding and characterisation of myeloma and its treatment and management.

### What is the Myeloma XII trial trying to find out?

The Myeloma XII trial has been developed on the back of results from another national myeloma trial called the Myeloma X trial. The Myeloma X trial showed that a second high-dose therapy and **autologous** stem cell transplant (HDT-SCT) slows down the **progression** of myeloma in comparison to treatment with more standard chemotherapy. Myeloma X also showed, however, that the **depth and duration of response** to the second HDT-SCT was inferior to those reported for the first HDT-SCT.

The purpose of the Myeloma XII trial is to see if using a novel drug called **ixazomib** can strengthen the effect of the

second HDT-SCT. The trial is looking at the depth of response following a second HDT-SCT when the **induction treatment** contains ixazomib, and also whether using ixazomib as part of **consolidation** and **maintenance** treatment following the second HDT-SCT can slow down the progression of myeloma i.e. improve the duration of response.

### Which myeloma patients are eligible to take part?

The Myeloma XII trial is for myeloma patients experiencing their first relapse and requiring treatment, and who have already had one previous HDT-SCT.

To take part in this trial, patients must also meet other eligibility criteria, which include but are not limited to:

- Patients must have had at least 12 months of remission or **stable disease** following their first HDT-SCT
- Patients must have no significant liver, kidney, lung or heart damage, and must have adequate blood count levels (e.g. neutrophils and platelets within an acceptable range)

## An overview of the trial

(see Figure 1 on page 10 for a visual overview of the trial)

- All patients will receive induction treatment with 4 – 6 cycles of ixazomib, thalidomide and dexamethasone (ITD). A cycle lasts 28 days
- Patients who achieve at least stable disease will be randomised to receiving either standard high-dose therapy (melphalan) or so-called ‘augmented’ high-dose therapy (melphalan and ixazomib) prior to stem cell transplantation
- All patients who achieve at least a **minimal response** to HDT-SCT will undergo a second randomisation to consolidation and maintenance, or to no further treatment
- Patients randomised to consolidation and maintenance will receive 2 cycles of ITD and then a maintenance dose of ixazomib until the myeloma starts to become active again (relapse)

Neither patients nor their doctor can choose how patients will be randomised.

## What are the potential advantages and disadvantages of being in the trial?

Before deciding whether to take part in the Myeloma XII trial, it is important that patients understand what is involved so they can make an informed decision about whether or not to take part. This includes knowing and understanding what the trial involves and the potential advantages and disadvantages of taking part.

### Potential advantages:

- Ixazomib is not yet licensed as a treatment for myeloma in the UK but has been licensed in the US and other countries. Therefore being on the Myeloma XII trial gives UK patients an opportunity to receive this drug
- Neither consolidation nor maintenance treatment is approved for UK myeloma patients outside of a clinical trial setting so being on the Myeloma XII trial offers the opportunity, if randomised, to receive this type of treatment
- Having a second HDT-SCT has been shown to be advantageous in other clinical trials. For example, the Myeloma X trial showed

that a second HDT-SCT is more effective than standard chemotherapy in myeloma patients who have relapsed following their first HDT-SCT

- The Myeloma XII trial will be overseen by an expert committee whose role is to continually review the trial data being collected and to assess whether there are any issues that should be acted upon. If it becomes apparent that one of the treatment approaches is much better or worse than the other, the expert committee may consider stopping the trial early. In such cases all patients will have their treatment changed to the best available treatment
- Patients taking part are more closely monitored during and after the trial. This means that any changes – whether or not they are directly related to the trial treatment they are taking or to other factors – will be noticed and acted upon promptly

### **Potential disadvantages:**

- In the Myeloma XII trial patients are randomised to particular treatment pathways (a ‘standard treatment’ pathway or a ‘new treatment’ pathway).

Some patients may consider being randomised to the standard treatment pathway a potential disadvantage. However, it is worth bearing in mind that there is no guarantee the new treatments in the trial will work better than the standard treatments they are being compared to

- On a practical level, it is possible that patients may have to travel to another hospital to prepare for and have their second HDT-SCT. This may be a significant issue for some patients and their families
- Similarly, although most of the tests carried out as part of the monitoring process are the same as those for patients not taking part in the trial there may be some additional tests that are specific to the trial. This may require patients to go to hospital for tests more regularly than they are used to
- As with most treatments for myeloma, the treatments in this trial have the potential to cause side-effects. HDT-SCT in particular is an intensive treatment option and can put a significant physical and emotional strain on patients and their families. Patients in

this trial will all have had a prior HDT-SCT so will know in part what to expect, although the experience may be different (better or worse) the second time round. It is important that the potential side-effects and risks of treatment are acceptable to patients and do not affect their quality of life to the extent that the side-effects outweigh the benefits of treatment, either in the short term or long term

Taking part in the trial is entirely voluntary. Patients will still be entitled to the currently available treatment for myeloma that is most suitable for them if they decide not to take part. If patients decide to take part in the trial, they will be asked to sign an Informed Consent Form.

### **How long will treatment in the Myeloma XII trial last?**

The length of treatment depends on how patients are randomised and on their individual response to treatment. The length of the treatment phase including HDT-SCT is between 6 -12 months. Patients randomised to the consolidation and maintenance arm will receive consolidation treatment with ITD for 2 months then ixazomib maintenance

treatment until their myeloma shows signs of becoming active again (relapse). This will vary from patient to patient and could be a few months or several years.

### **What if a patient wants to withdraw from the trial?**

Patients are free to decide to withdraw from the Myeloma XII trial at any time, although some follow-up may be needed. If patients are already part way through treatment such as their second HDT-SCT, it may not be possible to leave the trial immediately due to the potentially serious effects of stopping part way through treatment.

If patients are considering withdrawing from the trial, they should discuss the implications of doing so and all other treatment options that may be available to them fully with their doctor or nurse.

### **What are the potential side-effects of the trial treatments?**

Some patients may have side-effects from the treatments they receive whilst on the Myeloma XII trial. These potential side-effects will be explained

to patients before treatment is started. Some of the more common side-effects of the treatments used are listed in the table below.

Side-effects vary considerably from patient to patient and the vast majority can be prevented. Those that do occur are usually mild and transient and can be treated and/or managed. If side-effects persist, treatment can be adjusted and the doses of the drugs patients receive can be reduced. In rare cases, if certain side-effects continue to persist after adjustments have been made, patients may be withdrawn from the trial.

If patients have any side-effects it is important that they tell their doctor or nurse as soon as possible so they can be managed and/or treated.

### **What tests/assessments are done as part of the trial?**

All patients are carefully monitored on a regular basis throughout the trial. Most of the tests carried out as part of the monitoring process are the same as those for patients not taking part in the trial, such as blood and urine tests. However, there are some additional tests that are specific to the trial.

<b>Treatment</b>	<b>Potential side-effects</b>
High-dose therapy (melphalan)	Nausea, vomiting, hair loss, mouth ulcers, diarrhoea, loss of appetite, infection, anaemia, bruising or bleeding, skin reactions, infertility
Thalidomide	Birth defects if taken during pregnancy, drowsiness, blood clots, skin rash, constipation, tingling or numbness in fingers/toes (peripheral neuropathy)
Steroids (dexamethasone)	Stomach irritation, increased appetite, swelling in hands and feet, increased blood sugar levels, infection, mood swings/irritability, difficulty in sleeping, muscle weakness
Ixazomib	Fatigue, nausea, vomiting, diarrhoea, skin rash, low platelet counts, peripheral neuropathy

For example, one of the aims of the Myeloma XII trial is to carry out tests to determine what bearing the genetic profile of patients' myeloma has on their outcomes and response to treatment.

Some of the additional genetic tests will require another Informed Consent Form to be signed – these optional tests will be explained to patients at the beginning of the trial.

When the trial treatment has finished, patients continue to be carefully monitored by their doctor. They will be asked to attend for regular check-ups (at least every 3 months) until the myeloma starts to become active again (relapse).

### **What happens if the treatment in the trial doesn't work?**

It may be that some patients do not respond well to the treatment they receive within the trial and that their myeloma is not brought under control. This is likely to be a disappointing time, both for patients and their families. If at any point during the trial the doctor thinks treatment is not working, the patient will be withdrawn from the trial and another treatment approach will be agreed upon and started.

### **Summary**

The results of the Myeloma XII trial will provide a greater understanding of whether the use of a novel drug called ixazomib can strengthen the effect of a second autologous stem cell transplant.

More specifically, the trial will provide important information on:

- Whether ixazomib can improve the depth of response to a second HDT-SCT when used as part of the induction treatment
- Whether ixazomib, when used as part of consolidation and maintenance treatment following a second HDT-SCT, can slow down the progression of myeloma
- What genetic factors contribute to patient outcomes and response to treatment

The results of the Myeloma XII trial will be used to inform clinical practice and the development of clinical guidelines for the treatment of myeloma.

The trial team will be looking at long-term outcomes of treatment which means that the final report, normally published in a medical journal, may not be available for several years after patients have completed the trial treatment. However, doctors involved in the

design of the trial will present interim results at national and international conferences throughout the trial. These will help shape the design of future myeloma clinical trials.

As new ways of treating myeloma become available, different questions about the best way to treat it will need to be answered.

Further national myeloma clinical trials will therefore follow.

There is no mandatory requirement to inform patients who take part in clinical trials of the results, but patients are very welcome to seek or request results when they are available from their doctor or from Myeloma UK.

### **Other information available from Myeloma UK**

Myeloma UK has a range of Essential Guides, Infoguides and Infosheets available covering many areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call the **Myeloma Infoline: 0800 980 3332** or **1800 937 773** from Ireland.

The Myeloma Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland. From outside the UK and Ireland, call **0131 557 9988** (charged at normal rate).

Information and support about myeloma is also available around the clock at **[www.myeloma.org.uk](http://www.myeloma.org.uk)**

## Glossary

### ■ Autologous

A patient's own stem cells are used, rather than a donor's

### ■ Consolidation

Further treatment which is given over a short period of time after the main treatment has finished with the aim of deepening the response

### ■ Depth of response

A measurement of the reduction in paraprotein or light chains in response to treatment

### ■ Duration of response

The length of remission or plateau before relapse

### ■ Induction treatment

Treatment with an initial standard-dose treatment combination that patients receive before a stem cell transplant procedure. Induction treatment aims to reduce the amount of myeloma in the bone marrow before the stem cells are collected

### ■ Ixazomib

A type of proteasome inhibitor drug which is given orally. Its trade name is Ninlaro®

### ■ Maintenance

Further treatment which is given over an extended period of time after the main treatment has finished, often at a lower dose, to prolong remission/plateau

### ■ Minimal response

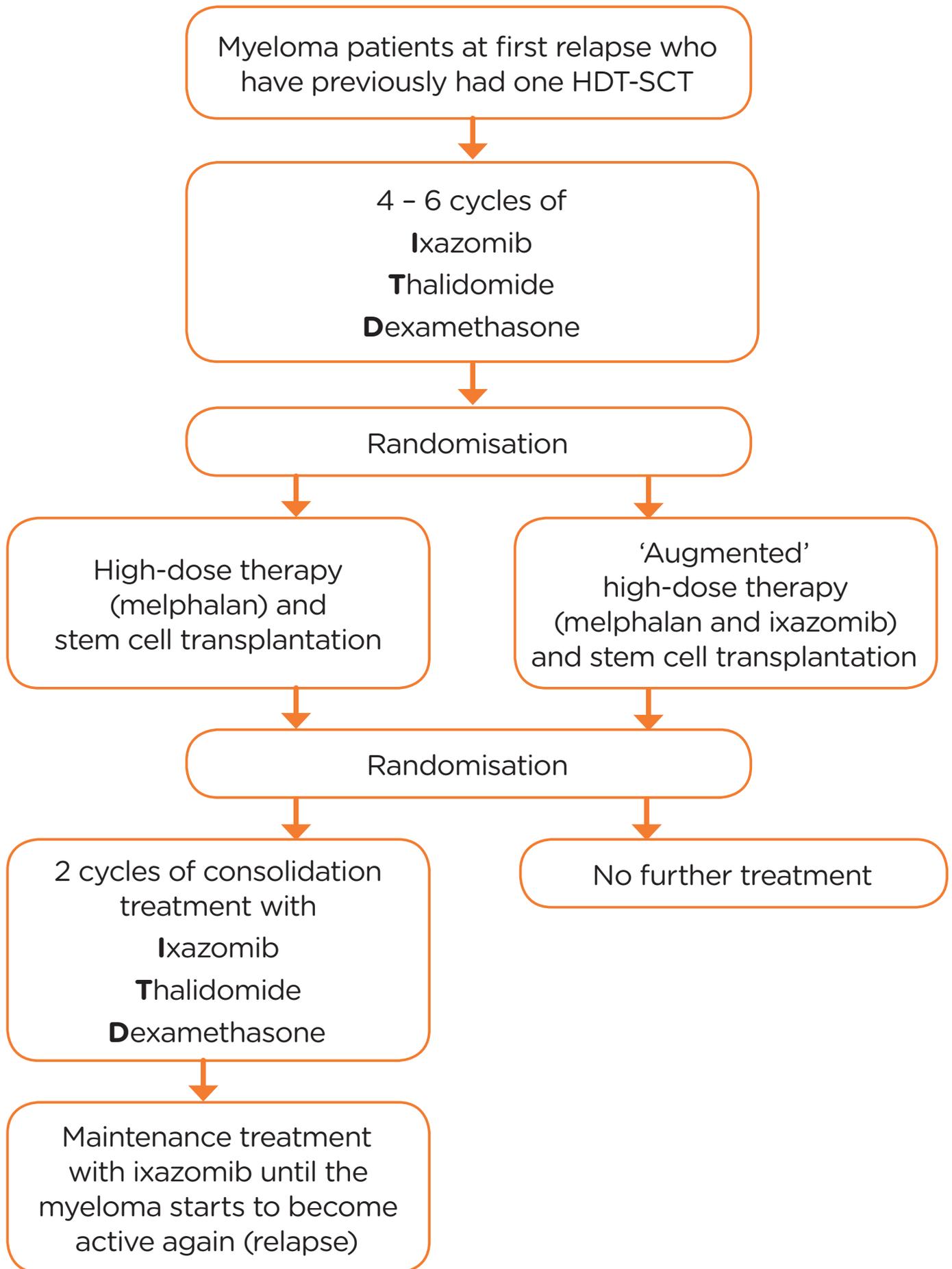
Between 25 - 49% reduction in paraprotein or light chain levels

### ■ Progression

An increase in the activity of the myeloma e.g. an increase in the paraprotein or light chain levels, or the development of new myeloma-related symptoms

### ■ Stable disease

A period of remission or plateau



**Figure 1** Overview of the Myeloma XII trial

# Notes

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**Myeloma Awareness Week 21 - 28 June**