Isatuximab (Sarclisa®)

Horizons Infosheet
Clinical trials and novel drugs

This Horizons Infosheet contains information on isatuximab, also known as Sarclisa®, a drug being investigated for the treatment of myeloma.

The Horizons Infosheet series provides information relating to novel drugs and treatment strategies that are currently being investigated for the treatment of myeloma. The series also aims to highlight the considerable amount of research currently taking place in the field of myeloma.

The drugs and treatment strategies described in the Horizons Infosheets may not be licensed and/or approved for use in myeloma. You may, however, be able to access them as part of a clinical trial.

What is isatuximab?

Isatuximab is a new drug being investigated for the treatment of myeloma.

Isatuximab is a monoclonal antibody drug. It attaches to a specific protein present on the surface of myeloma cells.

What is a monoclonal antibody?

Monoclonal antibodies are a class of drug being investigated in the treatment of myeloma.

Monoclonal antibodies are made in the laboratory to mimic the antibodies that your own immune system produces in response to foreign organisms (such as bacteria) that enter the body. Antibodies recognise proteins on the surface of harmful or abnormal cells and flag them for destruction by the immune system.

Monoclonal antibody drugs are designed to recognise and attach to specific proteins on the surface of cancer cells. 'Monoclonal' means all one type. This means that each group of monoclonal antibodies is made up of identical copies of one type of antibody and recognises one particular protein.

For more information see the **Immunotherapy Horizons Infosheet** from Myeloma UK

How does isatuximab work?

Myeloma cells produce a protein called CD38 on the cell surface. Isatuximab attaches to the CD38 protein, enabling the immune system to target and destroy the cell (Figure 1).

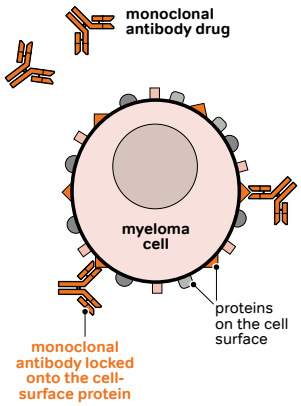

Figure 1. Mechanism of action of monoclonal antibody drugs

How is isatuximab given?

Isatuximab is given by intravenous infusion (into a vein). It is normally given at a dose of 10 milligrams per kilogram of body weight (10 mg/kg) on days 1, 8, 15 and 22 in the first 28 day cycle, then on days 1 and 15 in subsequent cycles.

Isatuximab has been shown to be most effective when used in combination with other anti-myeloma drugs.

What evidence exists to support the use of isatuximab?

The Phase III ICARIA trial investigated isatuximab in combination with pomalidomide (Imnovid®) and dexamethasone compared to pomalidomide

and dexamethasone alone. The trial included 307 relapsed and refractory myeloma patients who had had at least two previous lines of treatment that included lenalidomide (Revlimid®) and a proteasome inhibitor, such as bortezomib (Velcade®).

The median progression free survival (average length of time following treatment before the myeloma returns and further treatment is required) was 11.5 months for patients who received the isatuximab combination compared to 6.5 months for patients who received pomalidomide and dexamethasone alone.

What are the possible known side effects of isatuximab?

The most commonly observed side effects of isatuximab include:

- Infusion reaction. This can occur during or after infusion. Signs may include shortness of breath, high blood pressure, cough, chills or nausea. Before isatuximab is infused, patients will be given supportive treatment to protect against these reactions
- Reductions in red or white blood cells or platelets
- Upper respiratory tract infections, pneumonia or bronchitis
- Diarrhoea

Is isatuximab currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving isatuximab, visit the Myeloma Trial Finder on **myeloma.org.uk**

To be enrolled on a clinical trial, patients have to meet certain conditions known as eligibility criteria. You should speak to your doctor in the first instance if you are interested in taking part in a trial.

If you are considering taking part in a clinical trial your doctor will discuss in detail the risks and benefits for you. They will give you detailed information to enable you to make an informed decision about whether to take part.

Availability of isatuximab in the UK

Isatuximab is not currently available for use in myeloma in the UK and is only accessible to patients as part of a clinical trial.

Before a drug can be widely used, it must first be licensed as a safe and effective treatment. This is usually done by regulatory authorities

at a European level and involves a review of evidence from large-scale clinical trials. Isatuximab was licensed in June 2020 for use in Europe, for patients with relapsed/refractory myeloma in combination with pomalidomide (Imnovid®) and dexamethasone.

Normally, the licensed drug must then be approved by a UK drug appraisal body before it can be routinely prescribed by NHS doctors. The drug appraisal process differs from licensing. It looks at how effective the newly-licensed drug is compared with existing drugs already in use on the NHS, and decides whether the drug offers the NHS good value for money.

The main body responsible for carrying out drug appraisals in England and Wales is the National Institute for Health and Care Excellence (NICE). Isatuximab is currently undergoing an appraisal process with NICE.

NICE recommendations are usually adopted in Northern Ireland. Scotland's drug appraisal body is the Scottish Medicines Consortium (SMC), who have not yet appraised isatuximab.

Future directions

Isatuximab continues to be studied in different patient groups and in various treatment combinations. This includes relapsed and/or refractory patients and newly diagnosed patients.

In addition to pomalidomide and dexamethasone, isatuximab is currently being investigated in

combination with other treatments, such as bortezomib, carfilzomib and lenalidomide.

These studies will provide information about the most effective ways to use isatuximab in myeloma.

Key points

- Isatuximab is a drug that is being investigated in the treatment of myeloma.
- Isatuximab is a monoclonal antibody drug which targets the CD38 protein found on the surface of myeloma cells
- Clinical trials are investigating isatuximab in combination with other anti-myeloma drugs for relapsed and refractory patients and for newly diagnosed patients

- Side effects seen so far include infusion reaction, reduced white blood cells, infections and diarrhoea
- Isatuximab is not yet widely available in the UK because it has not been approved for use on the NHS. However, patients may be treated with it as part of a clinical trial

About this Infosheet

The information in this Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation.

For a list of references used to develop our resources, visit myeloma.org.uk/references

We value your feedback about our patient information.
For a short online survey go to myeloma.org.uk/pifeedback
or email comments to myelomauk@myeloma.org.uk

Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all aspects of myeloma, its treatment and management. Download or order them from myeloma.org.uk/publications

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma Infoline on 0800 980 3332 or 1800 937 773 from Ireland.

The Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at myeloma.org.uk

Notes

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MyelomaUK

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Call the Myeloma Infoline on
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Registered Charity No: SC026116

Published by:	Myeloma UK
Publication date:	December 2019
Last updated:	July 2020
Review date:	January 2021

Myeloma Awareness **Week** • **21–27** June