Belantamab mafodotin

Horizons Infosheet
Clinical trials and novel drugs

This Horizons Infosheet contains information on belantamab mafodotin (previously known as GSK2857916), 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 belantamab mafodotin?

Belantamab mafodotin is a new drug being investigated for the treatment of myeloma. It is a type of drug known as an antibody-drug conjugate.

What are antibody-drug conjugates?

Antibody-drug conjugates consist of two parts joined together:

- A monoclonal antibody
- A chemotherapy drug (a drug intended to kill cancer cells)

What is a monoclonal antibody?

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) or abnormal cells. Antibodies recognise proteins on the surface of harmful or abnormal cells and flag them for destruction by the immune system.

Monoclonal antibodies are designed to recognise and attach to specific proteins on the surface of abnormal cells such as myeloma 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.

Monoclonal antibody drugs can be used to treat cancers including myeloma, for example daratumumab (Darzalex®) is a monoclonal antibody drug licensed for treatment of myeloma. Monoclonal antibodies also form part of antibody-drug conjugates.

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

How do antibody-drug conjugates work?

Antibody-drug conjugates work in two main ways.

Firstly, antibody-drug conjugates act as a "delivery system" for a chemotherapy drug. The monoclonal antibody part recognises and attaches to a specific protein on a cell. The chemotherapy drug linked to the antibody can then enter that cell directly.

As well as delivering the chemotherapy, the monoclonal antibody in the antibody-drug conjugate flags the cell for the body's immune system to destroy.

The way antibody-drug conjugates work is shown in Figure 1.

How does belantamab mafodotin work?

The monoclonal antibody (belantamab) recognises a protein on the surface of myeloma cells called BCMA. Myeloma cells have a lot of BCMA on their surface, while healthy cells have very little. This means that the belantamab can effectively target myeloma cells, and the effects on healthy cells are minimised.

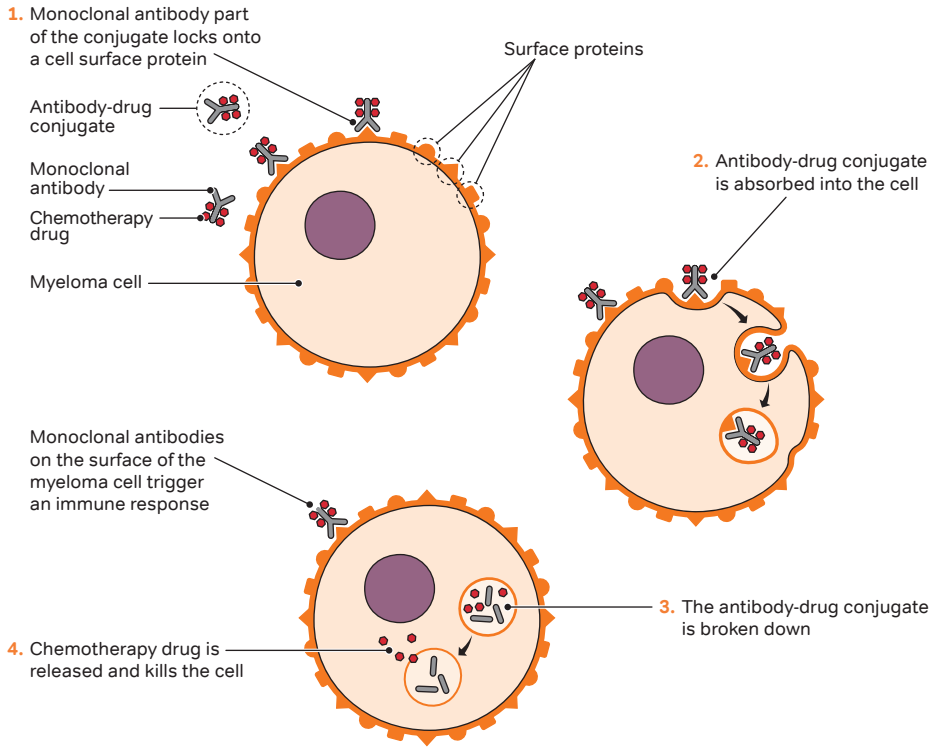

Figure 1. Mechanism of action of antibody-drug conjugates in myeloma

The chemotherapy drug linked to the belantamab is called mafodotin. It works by stopping normal cell processes in actively dividing cells and causing cell death. Mafodotin is too toxic to be given on its own – the linker attaching it to the belantamab stops it being released in the body until it is inside a myeloma cell.

Once the belantamab has recognised the BCMA on the surface of a myeloma cell and attached to it, the belantamab mafodotin is absorbed into the myeloma cell, and the mafodotin is then released and acts to kill the cell.

The belantamab attached to the BCMA on the cell surface also triggers an immune response against the myeloma cells.

How is belantamab mafodotin given?

Belantamab mafodotin is given as an intravenous infusion (into the vein). The dosage in clinical trials

has varied. The usual dose now is 2.5 milligrams of drug per kilogram of body weight (2.5mg/kg), given every three weeks.

What evidence exists to support the use of belantamab mafodotin?

Belantamab mafodotin is currently being investigated for the treatment of relapsed and/or refractory myeloma patients.

In a phase I trial called DREAMM-1, belantamab mafodotin was first given to small numbers of relapsed/refractory myeloma patients at different doses, starting with very low doses, to check how well the drug was tolerated and how long it remained in the body. After this, a dose of 3.4mg/kg was selected for the second part of the trial. This dose was given to 35 patients with relapsed/refractory myeloma and several previous lines of treatment. In this part of the trial, 21 of the 35 patients (60%) had a partial response or better to the treatment. The median progression-free survival (time before the myeloma started to come back) was 12 months.

In the phase II trial DREAMM-2, 196 patients were divided into two groups and given 2.5 or 3.4mg/kg belantamab mafodotin. The patients had relapsed and/or refractory myeloma, and had received three or more previous lines of treatment. They were all either refractory to daratumumab, or could not receive daratumumab. Initial findings were that 30 of 97 patients in the 2.5mg/kg group (31%) and 34 of 99 patients in the 3.4mg/kg group (34%) had a partial response or better to the treatment.

What are the possible known side effects of belantamab mafodotin?

In clinical trials of belantamab mafodotin side effects seen to date have included:

- Effects on the cornea (surface of the eye)
- Reduced numbers of platelets in the blood
- Anaemia
- Infusion reactions
- Increase in a blood enzyme called aspartate aminotransferase
- Nausea

Because belantamab mafodotin is a relatively new drug, new side effects may emerge which have not yet been reported.

Is belantamab mafodotin currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving belantamab mafodotin, visit the Myeloma Trial Finder at trials.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 belantamab mafodotin in the UK

Belantamab mafodotin is not currently licensed 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.

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 compares how effective the newly-licensed drug is to existing drugs already in use on the NHS and decides whether it 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). NICE recommendations are usually adopted in Northern Ireland. Scotland's drug appraisal body is the Scottish Medicines Consortium (SMC).

Future directions

A larger clinical trial is planned, which will compare belantamab mafodotin with a standard myeloma treatment, in patients with relapsed and/or refractory myeloma who have had several previous lines of treatment.

Clinical trials are also planned which will look at combinations of belantamab mafodotin with other anti-myeloma drugs.

Key points

- Belantamab mafodotin is a new drug being investigated for the treatment of myeloma
- Belantamab mafodotin is type of drug called an antibody-drug conjugate
- The drug contains a monoclonal antibody which targets proteins called BCMA on myeloma cells. This is linked to a chemotherapy drug
- The chemotherapy drug is delivered direct to myeloma cells, and once inside them can kill them
- Belantamab mafodotin has shown anti-myeloma effects in patients with relapsed and/or refractory myeloma who have received several previous lines of treatment, and further clinical trials are underway or planned
- Side effects seen so far with belantamab mafodotin have included effects on the surface of the eye, lower levels of platelets in the blood, and anaemia
- Belantamab mafodotin is not yet widely available because it has not been licensed and approved for use in myeloma. However, patients may be treated with it through 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.

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For a short online survey go to myeloma.org.uk/pifeedback
or email comments to myelomauk@myeloma.org.uk

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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

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We're here for everything a diagnosis of myeloma brings

Get in touch to find out more about how we can support you

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