Bispecific antibodies

Horizons Infosheet
Clinical trials and new treatments

This Horizons Infosheet contains information on bispecific antibodies, a type of treatment being investigated for use in myeloma.

The 'Horizons Infosheet' series provides information about new drugs and treatments that are 'on the horizon' – ones that are currently being investigated for use in myeloma. The series also aims to highlight the large amount of research currently taking place.

The treatments 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 are bispecific antibodies?

Bispecific antibodies are a new type of treatment being investigated for use in myeloma and other types of cancer. They are also called T cell engagers. Bispecific antibodies are part of a group of treatments called immunotherapies. Immunotherapies are treatments that help the immune system to recognise and kill cancer cells.

For more information about other immunotherapies see the **Immunotherapy in myeloma Horizons Infosheet** from Myeloma UK

Bispecific antibodies are manufactured in a laboratory. They are similar to our own antibodies, which bind to proteins on the surface of abnormal cells in our bodies, to flag them for removal.

What makes bispecific antibodies different is that they work by binding to two different types of cell at the same time. They recognise and bind to:

- A protein on a cancer cell (such as a myeloma cell)
- A protein on the body's own T cells. T cells are a type of white blood cell that plays an important part in the body's immune system. One type of T cell can kill abnormal cells in the body, including cancer cells

There are several bispecific antibodies being developed for treatment of myeloma. These include:

- Teclistamab
- Talquetamab
- Cevostamab
- Elranatamab
- Linvoseltamab

These bispecific antibodies differ in the proteins they target on myeloma cells, but the way they all work is similar and is explained in the next section.

How do bispecific antibodies work?

When bispecific antibodies bind both to myeloma cells (or other cancer cells) and to T cells, the patient's T cells are brought into close contact with the myeloma or other cancer cells. The T cells are then made active and are able to kill the myeloma cell or other cancer cell.

This is shown in Figure 1 on the next page. The diagram shows a myeloma cell and a T cell, and the coloured blobs are the proteins on the surface of the cells. A bispecific antibody (shaped like a Y) is binding to both of the cells. One arm of the Y

(shown in orange) is binding to a protein on the myeloma cell, and the other arm (shown in blue) is binding to a protein on the T cell. This is bringing the myeloma cell and the T cell close together, so that the T cell can kill the myeloma cell.

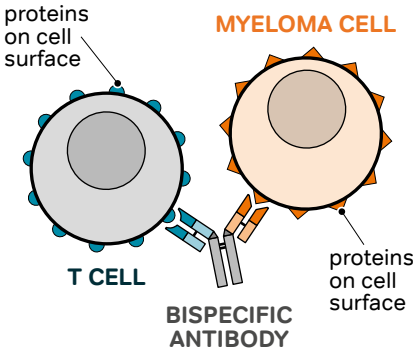

Figure 1. A bispecific antibody binding to a myeloma cell and a T cell. The T cell is brought into close contact with the myeloma cell, it is made active, and it attacks the myeloma cell.

How are bispecific antibodies given?

Bispecific antibodies are given as a subcutaneous injection (under the skin) or an intravenous infusion (into a vein). They are often given once a week or every other week. The dosage and schedule of dosing will differ depending on the particular bispecific antibody, and may vary between different clinical trials.

What evidence exists to support the use of bispecific antibodies?

Some of the clinical trials which have so far been done are described below. The clinical trials report the number of patients who had a 'response to treatment'. Response to treatment is measured by standard myeloma test results. All the trials were in patients with relapsed and/or refractory myeloma, who had received a number of previous treatments.

In a trial called MajesTEC-1, teclistamab was given to 165 patients. 104 of the 165 patients (63%) responded to the treatment. The time before their myeloma started to come back was 11 months on average.

In a trial called MonumenTAL-1, patients were given talquetamab at two different doses. 21 of the 30 patients in the first dose group (70%), and 28 of the 44 patients in the second dose group (64%) had a response to the treatment.

In a trial called MagnetisMM-3, elranatamab was given to 123 patients. 75 of the patients (61%) responded to the treatment, and in about half of those patients, their myeloma had still not returned after 15 months.

What are the possible known side effects of bispecific antibodies?

Side effects reported to date have included:

- Reduced numbers of white blood cells, red blood cells or platelets, and reduced levels of antibodies in the blood. These effects are common and can be severe
- Anaemia. This can happen if the number of red blood cells is reduced
- Infections. These are common and can be severe
- A potentially serious reaction called cytokine release syndrome (CRS). This can cause symptoms such as fever, shortness of breath and changes in blood pressure
- Neurological symptoms such as confusion, disorientation and headache, which may be signs of a potentially serious syndrome called ICANS (immune effector cell-associated neurotoxicity syndrome)
- Changes in blood chemistry
- Gastrointestinal symptoms (nausea, diarrhoea, constipation or altered sensations of taste)
- Damage to the nerves called peripheral neuropathy
- Fatigue
- Changes to the skin and nails

Although some of these side effects can potentially be serious and severe, patients are given pre-treatments to help prevent side effects. Patients are monitored for side effects, and are treated for any that do occur. Bispecific antibodies are generally given at a low dose to start with, to reduce the risk and severity of side effects such as CRS and ICANS.

Because bispecific antibodies are a relatively new group of treatments, new side effects may emerge which have not yet been reported.

Are bispecific antibodies currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving bispecific antibodies, 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. These are for the protection of patients and are an important part of the trial design.

For more information about taking part in clinical trials, see the **Clinical trials and how treatments are developed Infoguide** from Myeloma UK.

You should speak to your doctor in the first instance if you are interested in taking part in a clinical trial. Your doctor will discuss 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 bispecific antibodies in the UK

Before any new treatment can be widely used on the National Health Service (NHS) in the UK, it goes through two processes:

- Licensing – the new treatment is licensed as safe and effective, and can be prescribed by doctors. Licensing is based on the results of clinical trials and other information about the treatment. The main licensing body in the UK is the Medicines and Healthcare products Regulatory Agency (MHRA)
- Approval – the licensed treatment is approved for general use on the NHS. Approval is based on clinical effectiveness and cost-effectiveness. Two of the appraisal bodies in the UK, that approve drugs for use on the NHS, are the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC)

For more information about treatment licensing and approval, see the **Clinical trials and how treatments are developed Infoguide** from Myeloma UK

Bispecific antibodies are not yet in general use for myeloma on the NHS in the UK, because none of them have completed both of these two processes. However, they may be accessible to patients as part of a clinical trial.

The bispecific antibodies teclistamab (Tecvayli®), talquetamab (Talvey®) and elranatamab (Elrexfio®) have been licensed by the MHRA for use in myeloma in the UK. However, none of these have been approved for use on the NHS. They may be available on a private prescription, although this can be very costly. Elranatamab may be available to patients through an expanded access scheme (also known as

a compassionate use scheme). Requests for expanded access can only be made by a haematologist.

Future directions

Bispecific antibodies for myeloma are an active area of research. Researchers are continuing to build up their understanding of the most effective ways to use them, and of side effects that can occur.

Some of the questions being asked by researchers are:

Which proteins on the myeloma cell can be targeted?

Bispecific antibodies are being developed that target different proteins on the myeloma cell.

When and how are bispecific antibodies best used?

Initial clinical trials into new myeloma treatments (including bispecific antibodies) tend to be in patients who have had a number of previous treatments and relapses, and who may therefore have limited treatment options.

However, researchers are also looking at using bispecific antibodies at earlier stages of myeloma, when patients' immune systems and T cells are 'fitter'. Some clinical trials of bispecific antibodies are therefore being done at earlier stages of myeloma. This research is at an early stage, however. Most clinical trials of bispecific antibodies are in patients with relapsed and/or refractory myeloma, who have had several previous lines of treatment.

Clinical trials are also looking at whether bispecific antibodies work better when combined with other myeloma treatments that work in different ways.

Researchers are continuing to look at the best way to use bispecific antibodies in order to minimise side effects, and how best to manage any side effects that do occur.

In particular, researchers are looking at the number and severity of infections that occur with bispecific antibodies. They are looking at the types of infections, and the best ways to avoid or manage them. This may include giving prophylactic (preventative) treatments, and modifying the dosing schedule (for example reducing the length of treatment or having treatment-free intervals).

There is some evidence that changing the dosing schedule of bispecific antibodies may reduce the number of side effects that occur, without necessarily

reducing the effectiveness of the treatment. This is an area of research at present.

How and why do bispecific antibodies stop working?

Eventually, bispecific antibodies will stop working. This may be because:

- The myeloma cells may no longer have the protein on their surface that the bispecific antibody can bind to. This is one of the ways that myeloma cells can evolve and become more resistant to treatment
- The T cells may become 'exhausted' in various ways, so that they are not as active
- A type of T cells called regulatory T cells (Tregs) may become more active. Tregs are a different type of T cell. They work by preventing the immune system from becoming overactive. However, if Tregs become too active they may stop bispecific antibodies working so well
- There may be changes in the ways myeloma cells, immune system cells and bone marrow cells interact. These interactions are complex, and changes in the interactions can make it more difficult for the T cells to kill the myeloma cells

Researchers are looking for different ways to overcome these factors, so that bispecific antibodies can work better for longer.

For example, targeting two different proteins on the myeloma cell may mean that the treatment is less likely to stop working if the myeloma cells no longer have one or the other of the proteins on their surface.

A clinical trial is currently underway in which patients are given two bispecific antibodies as a combination treatment. The two treatments (teclistamab and talquetamab) target different myeloma surface proteins.

So-called 'trispecific antibodies' are at an earlier stage of development, but are beginning to be tested in clinical trials. These can bind to two different target proteins on the myeloma cell, as well as binding to T cells.

Key points

- Bispecific antibodies are a new group of treatments being investigated for use in myeloma
- There are several bispecific antibodies in development for treatment of myeloma
- Bispecific antibodies attach to myeloma cells and to cells in the immune system called T cells
- Bispecific antibodies bring the T cells into close contact with myeloma cells. The T cells are then made active, and are able to kill the myeloma cells
- Bispecific antibodies have shown anti-myeloma effects in a number of clinical trials in patients with relapsed and/or refractory myeloma, and further clinical trials are underway or planned
- Side effects seen so far with bispecific antibodies have included infections, fever, reduced levels of blood cells, reduced blood pressure, neurological symptoms, gastrointestinal symptoms, altered taste, and changes to skin or nails
- No bispecific antibodies have been approved for use on the NHS in the UK. However, patients may be treated with them as part of a clinical trial

About this Infosheet

The information in this Infosheet is not meant to replace the advice of your healthcare 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 patientinfo@myeloma.org.uk

Other information available from Myeloma UK

Myeloma UK has a range of information booklets available covering all aspects of myeloma and related conditions. 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

MyelomaUK

We're here for everything a diagnosis of myeloma brings

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

Call the Myeloma Infoline on
0800 980 3332

Email Ask the Nurse at
AskTheNurse@myeloma.org.uk

Visit our website at
myeloma.org.uk

Trusted Information Creator
Patient Information Forum

Myeloma UK
22 Logie Mill, Beaverbank Business Park,
Edinburgh EH7 4HG
0131 557 3332
myelomauk@myeloma.org.uk
Registered Charity No: SC026116

Published by:	Myeloma UK
Publication date:	April 2024
Last updated:	April 2024
Review date:	April 2025