

Darzalex[®] (daratumumab)

This Horizons Infosheet contains information on Darzalex (also known as daratumumab), a drug being investigated for the treatment of myeloma.

The Horizons Infosheet series provides information relating to novel drugs 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 drug development.

The drugs 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 Darzalex?

Darzalex is a new drug being investigated for the treatment of myeloma. Darzalex is a monoclonal antibody which attaches specifically to a protein that is 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. 'Monoclonal' means all one type. This means that each group of monoclonal antibodies is made up of identical copies of one type of antibody.

Monoclonal antibodies are designed to recognise and attach to specific proteins on the surface of cancer cells. Each group of monoclonal antibody recognises one particular protein.

How does Darzalex work?

Myeloma cells produce a protein called CD38 which is present on the cell surface. Darzalex attaches to the CD38 protein found on the surface of myeloma cells, enabling the immune system to target and destroy it. See Figure 1.

How is Darzalex given?

Darzalex is given by intravenous infusion (into a vein) over a number of hours. The recommended dose when used

as a monotherapy (used on its own and not in combination with other drugs) is 16 milligram per kilogram (mg/kg) which is given once a week for the first 8 weeks. From week 9 to week 24, Darzalex is given every 2 weeks, and then every 4 weeks. Treatment continues for as long as the patient benefits from it.

Darzalex has shown to be effective as a monotherapy. It is also being trialled in combination with other anti-myeloma treatments such as dexamethasone, Velcade[®] (bortezomib) and Revlimid[®] (lenalidomide).

Trials are being carried out in both newly diagnosed and relapsed and/or refractory patients.

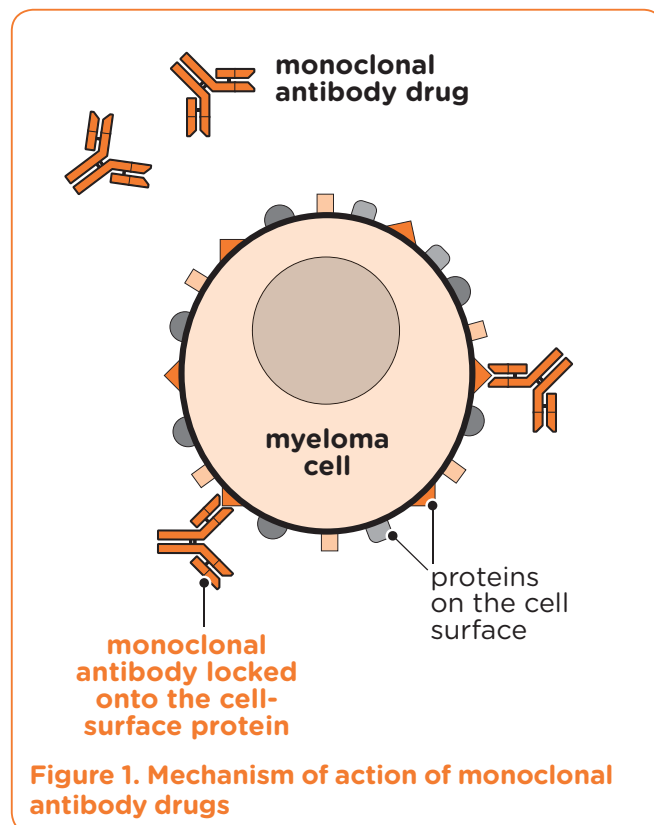


Figure 1. Mechanism of action of monoclonal antibody drugs

What evidence exists to support the use of Darzalex?

Initial findings from the Phase III CASTOR trial, comparing Darzalex in combination with Velcade and dexamethasone to Velcade and dexamethasone in 500 relapsed and/or refractory myeloma patients, have shown that the number of patients responding to treatment increased by adding Darzalex to Velcade and dexamethasone (from 63% to 83%). Furthermore, the addition of Darzalex is expected to at least double progression free survival (the length of time following treatment before myeloma returns and further treatment is required) in patients.

The Phase III POLLUX trial is investigating Darzalex, Revlimid and dexamethasone compared to Revlimid and dexamethasone in relapsed and/or refractory patients. By adding Darzalex to Revlimid and dexamethasone, the number of patients responding to treatment increased (from 76% to 93%) and also doubled the rate of complete response (where the response to treatment results in less than 5% plasma cells in the bone marrow) compared to Revlimid and dexamethasone

alone. Initial findings also show a 63% reduction in the risk of disease progression when patients were treated with Darzalex, Revlimid and dexamethasone compared to Revlimid and dexamethasone.

What are the possible known side-effects of Darzalex?

The most commonly observed side-effects of Darzalex occur within three to four hours of receiving the intravenous infusion. These include fever, chills, cough, nausea, changes in blood pressure, flushing, rash and fatigue. These are typically more likely to occur with the first infusion rather than second or subsequent.

Other side-effects reported include: low white blood cell levels (lymphopenia); low platelet levels (thrombocytopenia); low red blood cell levels (anaemia) and elevated liver enzymes.

Is Darzalex currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving Darzalex, visit the Myeloma Trial Finder on www.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.

Availability of Darzalex in the UK

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).

Darzalex has been granted a licence by the European Medicines Agency (EMA) for use across Europe as a monotherapy in relapsed and/or refractory myeloma patients.

The EMA is currently considering an application to broaden out the Darzalex licence, so that it can be used in combination with Revlimid and dexamethasone, or Velcade and dexamethasone, in relapsed and/or refractory patients.

Darzalex is also now being assessed by the UK drugs appraisal bodies to determine whether it can be approved and made available for use by NHS doctors.

Future directions

Darzalex continues to be studied in different patient groups and in different treatment combinations.

These trials will provide information about the safest and most effective way to use Darzalex in myeloma.

About this Horizons Infosheet

The information in this Horizons 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. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication.

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**

Notes

Notes

Published by: Myeloma UK
Publication date: June 2013
Last updated: December 2016
Review date: June 2017

Myeloma UK 22 Logie Mill, Beaverbank Business Park, Edinburgh EH7 4HG
T: 0131 557 3332 **E: myelomauk@myeloma.org.uk** Charity No: SC 026116

Myeloma Infoline: 0800 980 3332 or
1800 937 773 from Ireland
www.myeloma.org.uk

Myeloma Awareness Week 21 - 28 June