Venetoclax (Venclyxto®)

Horizons Infosheet
Clinical trials and novel drugs

This Horizons Infosheet contains information on venetoclax, a drug being investigated for the treatment of patients with the t(11;14) type 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 novel 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 venetoclax and how does it work?

Venetoclax (also known as Venclyxto®) is a new type of drug being investigated for the treatment of myeloma. It is being investigated specifically for patients with a genetic type of myeloma called t(11;14).

Venetoclax belongs to a class of drugs known as pro-survival inhibitors. These work by speeding up cancer cell death. Venetoclax targets a protein called BCL-2, which is found in higher amounts in

myeloma cells than in healthy cells. The BCL-2 protein prevents so-called 'apoptosis' (programmed cell death) of some cells.

Myeloma cells exploit the BCL-2 protein to promote their survival, allowing them to keep growing and multiplying. Venetoclax inhibits the action of BCL-2. This then causes myeloma cells to die.

Why is venetoclax being investigated for t(11;14) myeloma only?

Myeloma is associated with multiple genetic abnormalities or subtypes. BCL-2 has been found to be present in higher amounts in the myeloma cells of patients with a specific genetic subtype called t(11;14). Correspondingly, venetoclax has been shown to work especially well in patients with the t(11;14) genetic subtype, and that means that the benefit of treatment is expected to outweigh the risk of possible side effects in this group of patients.

For more information see the **Genetics and myeloma Infoguide** from Myeloma UK

How is venetoclax given?

Venetoclax is an oral drug, given as a tablet. It is currently being investigated in Phase III clinical trials as a once-daily treatment of 800mg in myeloma.

Though venetoclax has been shown to work on its own (as a monotherapy), it has also been investigated in combination with other myeloma treatments such as dexamethasone.

What evidence exists to support the use of venetoclax?

Venetoclax is currently being studied in a number of different blood cancers, including myeloma. Initial trials in myeloma were not specifically for t(11;14) patients, but the benefits in these patients seemed to be greater than in other patients.

In a phase I clinical trial, 66 relapsed and/or refractory patients were treated with venetoclax monotherapy. Around half of the patients had the t(11;14) genetic subtype. 14 of the 66 patients (21%) had a partial (or better) response to the venetoclax (called 'overall response'). 12 of these 14 responders had the t(11;14) genetic subtype, so that the response rate in the t(11;14) patients was 12 out of 30 (40%).

In a trial of venetoclax combined with bortezomib and dexamethasone, the overall response rate was 44 out of 66 (67%) across all patients.

A larger scale trial called 'BELLINI' was set up to investigate venetoclax as combination treatment. 194 patients were given venetoclax with bortezomib and dexamethasone, and 97 were given placebo (dummy tablets) plus bortezomib and dexamethasone. Only a small number of the patients in this trial had the t(11;14) genetic subtype. Overall response rate was found to be better in the venetoclax group than in the group receiving bortezomib and dexamethasone only (82% compared with 68%). However, the safety profile was also less good in the venetoclax group.

Based on these trials, it has been decided that clinical trials should continue in patients with the t(11;14) genetic subtype specifically, as these are the patients where the benefit is expected to be greater, and where the benefit of treatment is likely to outweigh the risks.

What are the possible known side effects of venetoclax?

Venetoclax is a new treatment which can cause serious side effects. In clinical trials, between a third and half of patients had serious side effects. Side effects which have been reported so far in trials in myeloma have included diarrhoea, nausea, constipation, fatigue, neutropenia (low level of neutrophils, a type of white blood cell, which increases risk of infections), pneumonia, thrombocytopenia (low level of platelets) and anaemia.

Because venetoclax is not yet in widespread use in myeloma, new side effects may emerge which have not yet been reported.

Is venetoclax currently available in any UK clinical trials?

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

Venetoclax is currently being investigated in a clinical trial called 'CANOVA', in patients with the t(11;14) subtype of myeloma. Venetoclax is being compared with pomalidomide (Imnovid®) – both

are being given in combination with dexamethasone. The trial includes several centres in the 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 venetoclax in the UK

Venetoclax 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 the regulatory authorities at a European level and involves a review of evidence from large-scale clinical studies.

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).

For more information see the **Health Technology Assessment (HTA) Infosheet** from Myeloma UK

In 2016 venetoclax was granted "orphan drug designation" by the European Medicines Agency (EMA) for myeloma. This means that the EMA will offer the drug company certain financial incentives throughout the development and licensing process to enable venetoclax to become available to patients sooner.

Future directions

Research on venetoclax in myeloma aims to obtain better information on its effectiveness in patients with the t(11;14) subtype, in comparison with standard treatment.

Another drug of the same type as venetoclax (a 'pro-survival inhibitor' called S65487) is also being investigated in myeloma. It is currently at a very early stage of clinical trials, including at centres in the UK.

Summary

- Venetoclax is a new drug that is being investigated for the treatment of myeloma
- It is one of a new class of drugs for myeloma called "pro-survival inhibitors". These work by speeding up cancer cell death
- Venetoclax is being investigated for treatment of patients with the t(11;14) genetic type of myeloma. Studies have indicated that it is most effective in this subgroup of patients
- Venetoclax can cause serious side effects. Side effects so far reported have included reductions in blood cells and effects on the digestive system
- Venetoclax is not yet widely available, because it has not been licenced and approved for use in myeloma. 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 areas 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

MyelomaUK

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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