Selinexor

Horizons Infosheet
Clinical trials and novel drugs

This Horizons Infosheet contains information on selinexor, a drug being investigated for the treatment of myeloma.

What is selinexor?
Selinexor is the first in a new family of drugs known as Selective Inhibitor of Nuclear Export (SINE™) compounds. Selinexor works by blocking the action of a protein called XPO1 within the nucleus (centre compartment) of myeloma cells.

What is XPO1?
XPO1 (also known as Exportin 1) is a protein responsible for moving other proteins between different parts of the cell.

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.

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.
Cells are made up of two compartments called the cytoplasm and the nucleus, which are separated by a plasma membrane. Some proteins involved in the life cycle of the cell, for example so-called tumour suppressor proteins, are active only when located within the nucleus. Other proteins must be moved from the nucleus into the cytoplasm to become active. The compartment in which different proteins are located can therefore affect the growth and survival of the cell.

XPO1 is a transport protein responsible for moving proteins out of the nucleus of a cell into the cytoplasm. One of the characteristics of myeloma cells that makes them different from healthy cells is their high level of XPO1, which has been found to be essential for myeloma cell survival. Myeloma cells use XPO1 to move tumour suppressor proteins from the nucleus into the cytoplasm. This deactivates them and allows the myeloma cells to multiply uninhibited.

**How does selinexor work?**

Selinexor is the first myeloma drug developed to block the action of XPO1. By blocking XPO1, selinexor prevents myeloma cells from moving tumour suppressor proteins out of the nucleus and into the cytoplasm. The tumour suppressor proteins are then activated as normal within the nucleus of the myeloma cell, leading to controlled death of the myeloma cells.

**How is selinexor given?**

Selinexor is given in tablet form. It can be given on its own as a monotherapy but it has shown to be most effective when used in combination with other myeloma treatments such as dexamethasone.

The usual maximum dose of selinexor in current clinical trials is 80mg twice a week, or in some trials 100mg once a week.

**What evidence exists to support the use of selinexor?**

Early stage clinical trials to date have indicated that selinexor can produce improvements in patients who have relapsed and/or are refractory to other treatments. Trials comparing selinexor directly with other treatment combinations have not yet been completed.

The largest clinical trial of selinexor completed to date is the STORM trial part 2, which included 122 patients who were heavily pre-treated/refractory to other treatments. All the patients were treated with
selinexor 80mg and dexamethasone 20mg, both given twice-weekly. Just over a quarter of the patients responded to the combined treatment, with either a partial response (24 patients), very good partial response (6), or complete response (2). The average length the response lasted was 4.4 months.

Other clinical trials so far reported have been in smaller numbers of patients. An early small trial in 22 myeloma patients indicated that the response to selinexor was better when it was combined with dexamethasone than when given alone.

The Phase I/II STOMP trial is investigating selinexor and dexamethasone in combination with various other myeloma treatments (bortezomib, carfilzomib, lenalidomide, pomalidomide or daratumumab), in relapsed myeloma patients. The bortezomib (Velcade®) arm of this trial has been completed and published. In this arm, 40 patients were treated with selinexor (between 60 and 100 mg), dexamethasone and bortezomib. 25 of the 40 patients responded to treatment, and the average time before their myeloma progressed was nine months. Other arms of this trial are still ongoing.

What are the possible known side effects of selinexor?

Selinexor is a new treatment which can cause serious side effects. Side effects which have been reported so far include:

- Effects on the blood: low platelet counts and bleeding; anaemia; low white cell counts and infections; and reduced sodium in the blood
- Digestive effects: nausea, vomiting, diarrhoea, loss of appetite and weight loss
- Dizziness, confusion and fatigue

In a number of patients in trials, side effects have been severe enough to require reduction of the drug dose or stopping treatment.

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

Is selinexor currently available in any UK clinical trials?

Most selinexor clinical trials are being done in patients who have had multiple relapses and treatments, and for whom existing treatment options are limited, rather than patients at earlier stages of their treatment pathway.
For an up-to-date list of UK clinical trials involving selinexor, 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 selinexor in the UK**

Selinexor 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 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 looks at how effective the newly-licensed drug is compared with 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 2014, selinexor was granted “orphan drug designation” by the European Medicines Agency (EMA) for myeloma. This means that the EMA will offer the drug company certain incentives to support the development and licensing process. Orphan designation is given for drugs thought to have potential to treat rare and serious conditions where there is a lack of alternative treatments. Orphan designation is not the same as licensing, and
further clinical trials still have to be done before the drug can be approved for use.

**Future directions**

Selinexor continues to be studied in different patient groups and in different drug combinations. It has an entirely different way of working from other anti-myeloma drugs, and therefore could have a place in the treatment of multiply relapsed and/or refractory patients. Studies are continuing of selinexor in combination with steroids and other anti-myeloma drugs. These trials will combine to provide better information about the benefits and safety of selinexor in myeloma.

A new trial developed with Myeloma UK started in 2018. It is looking at the combination of selinexor, cyclophosphamide and prednisolone, compared with cyclophosphamide and prednisolone alone, in patients who have relapsed after two or more previous drug treatments.

Selinexor was approved in July 2019 for use in the USA for patients with relapsed or refractory myeloma who are resistant to multiple other treatments. This was a so-called “accelerated approval”, a process where the US drug approval body the Food and Drug Administration (FDA) can approve drugs for serious conditions where there is an unmet need due to a lack of other available drugs, and a reasonable expectation of clinical benefit to patients. The approval is an interim measure and larger scale studies are underway to provide more evidence on the benefits and side effects of selinexor. This includes the larger BOSTON trial which has recruited patients at UK centres as well as in a number of other countries. The BOSTON trial is looking at whether selinexor in combination with bortezomib and dexamethasone is more effective than bortezomib and dexamethasone alone, in patients with relapsed and refractory myeloma.

**Summary**

- Selinexor is a new drug that is being investigated for the treatment of myeloma
- Selinexor is the first in a new class of drugs called SINE™ compounds. It works by blocking the movement of particular proteins within cells. The aim is to use this to stop myeloma cells from multiplying out of control
- Clinical trials with selinexor have so far been promising, indicating a potential treatment option in patients with relapsed and
refractory myeloma. The amount of evidence so far available is limited however. Larger trials are now taking place, to provide further information about selinexor’s effectiveness and side effects, and to compare it with existing myeloma treatments.

- Selinexor can cause serious side effects, which have so far included effects on blood cell counts, digestive effects, and dizziness.
- Selinexor is not yet widely available, because it has not been licensed 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 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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