Myeloma Canada
InfoGuide Series

Myeloma Immunotherapy

MYELOMA CANADA

MAKING MYELOMA MATTER

www.myeloma.ca

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Myeloma Canada wishes to acknowledge and thank the many individuals in our community who provided their invaluable input.

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Introduction

Myeloma Canada's *Myeloma Immunotherapy InfoGuide* has been created specifically for people living with myeloma, their families and their caregivers. The goal of this InfoGuide is to help you better understand myeloma immunotherapy, how it compares to conventional myeloma therapies, and how immunotherapy uses your immune system to fight the disease. It also provides you with the names (non-exhaustive) of myeloma immunotherapy treatments in development so that you know what may be available to you for the treatment of your myeloma.

Some of the more technical or unusual words in this InfoGuide appear in ***bold italics*** the first time they're used and are explained in the **Glossary** starting on page 18. Don't be afraid to ask members of your or your loved one's healthcare team to explain any terms or concepts you may have trouble understanding.

Throughout your journey with myeloma, your healthcare team will provide you with a large amount of information about your potential treatment options. Early identification, assessment and the treatment of symptoms is key. You may find it helpful to write down any questions that you have along the way and share these with your healthcare team regularly. They are the best people to help you understand what is happening and guide you to make informed decisions.

Be an informed and cautious information consumer

Be cautious of information that comes your way. While books and the internet offer a wealth of information, not all of it is correct, it may not apply to your unique situation, and it may be confusing or misleading. Well-intended people may also try to offer you health advice without knowing the details of your condition and its treatment. Certain online support groups may also be helpful, but again be wary of possible misinformation. It's important to know that your source is reputable and to discuss what you read with your healthcare team. Never make any change to your treatment plan without checking with them first, for any symptom you're experiencing.

Be sure to visit myeloma.ca for reliable, up-to-date resources, support group information and more.

Drug Access Navigator

Thanks to advances in research, new molecules and targeted therapies to treat myeloma are being developed at an impressive rate, with more options available than ever before. In Canada, access to, and coverage for, these new treatments varies across provinces and territories, making it often confusing and overwhelming to get the information you need.

About Myeloma Canada

Myeloma Canada is a registered non-profit organization created by, and for, people impacted by multiple myeloma. As the only national organization exclusively devoted to the Canadian myeloma community, Myeloma Canada has been making myeloma matter since its founding in 2005.

Working with leading myeloma researchers and clinicians as well as other cancer organizations and local support groups across Canada and internationally, Myeloma Canada seeks to strengthen the voice of the Canadian myeloma community and improve quality of life for those impacted by myeloma through awareness, education, advocacy, fostering an empowered community and supporting clinical research to find a cure.

Myeloma Canada's goals:

- **Increase awareness** of the disease and its effects on the lives of patients and their families
- **Educate** patients, families and caregivers
- **Advocate** for access to new therapies, treatment options and healthcare resources
- **Empower** patients and caregivers through community engagement
- **Advance** clinical research and promote access to new drug trials in Canada

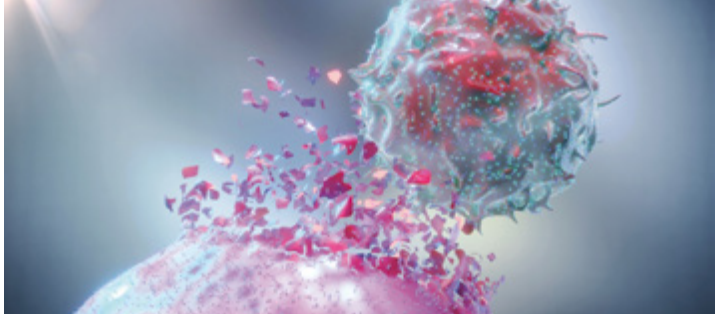
Myeloma Canada educational publications

For more detailed information about myeloma and living with the disease, visit myeloma.ca. From here, you can download Myeloma Canada's educational publications, watch educational videos, find a local support group and so much more.

Whether you're downloading a copy or requesting a printed version, all Myeloma Canada publications are free of charge. To order your printed copies of the materials below, email us at contact@myeloma.ca, or call us toll-free at 1-888-798-5771.

- *Multiple Myeloma Patient Handbook*
- *Multiple Myeloma Caregiver Handbook*
- *MGUS and Smouldering Multiple Myeloma*
- *Understanding Your Blood and Blood Tests*
- *Clinical Trials as a Treatment Option*
- *High-dose Therapy and Autologous Stem Cell Transplantation*
- *Myeloma Bone Disease*
- *Myeloma and the Kidney*
- *Managing Pain & Fatigue*
- *Amyloid Light Chain (AL) Amyloidosis InfoSheet*
- *Myeloma Immunotherapy*

Table of contents



What is myeloma immunotherapy?

What is myeloma immunotherapy?

Myeloma immunotherapy are treatments that work by stimulating the body's ***immune system*** to recognize and eliminate myeloma cells. Due to the complex nature of an immune system response and its various components, there are many potential ways it can be influenced by immunotherapy treatments.

The earliest example of myeloma immunotherapy is allogeneic (donor) ***stem cell transplantation*** (also known as ***bone marrow*** transplant) because it uses the immune system of a healthy matching donor – i.e., a relative (usually a sibling) or matched unrelated donor to attack myeloma cells in the recipient. Today, the approach remains an active area of research that is generally undertaken under the supervision of a ***clinical trial*** setting with a small number of select patients.

A healthy immune system

A healthy immune system is the body's natural defence against threats such as infections (e.g., bacteria, viruses), foreign particles, and even cancer. It consists of cells and tissues that respond to threats and work together to protect you. This process is known as an ***immune response.***

The body's ***white blood cells (WBCs; also called leukocytes)***, made by "blood-forming" or hematopoietic ***stem cells*** in the bone marrow, are the key components of the immune system. WBCs recognize harmful cells (i.e., infected or cancerous) and work to destroy them. The surface of all cells have specific proteins (***antigens***) that are unique and act as identity tags that stop the body from attacking its healthy cells.

Different types of WBCs each have different immune system functions. **Table 1** summarizes the immune system's key WBCs and their functions.

Table 1 – Key WBC components of the immune system

Cells	Function
 **Neutrophils**	▪ Target/detect chemical signals produced by bacteria and fungi ▪ Respond quickly to the first signs of infection ▪ Break down threats by engulfing them ***(phagocytosis)***
 **Macrophages**	▪ Target/detect chemical signals produced by bacteria and viruses ▪ Respond quickly to the first signs of infection ▪ Break down threats by engulfing them (phagocytosis)

Cells	Function
 **T lymphocytes (T-cells)**	▪ Recognize specific antigens on harmful cells ▪ Bind to harmful cells to surround and disable them ▪ Can transform into ***memory cells*** for long-lasting immunity There are three types of T-cells: - **T-helper cells:** Secrete small proteins (cytokines, see below) that stimulate ***B lymphocytes (B-cells)*** to mature into ***plasma cells*** and produce ***antibodies***; recognize foreign substances on antigen presenting cells, produce cytokines that signal other immune cells - **Regulatory T-cells:** Control immune reactions - **Cytotoxic T-cells**: Activated by infected cell and produce cytokines that kill the infected harmful cell
 **Natural killer (NK) cells**	▪ Recognize and destroy cells that have been infected by viruses or changed by cancer ▪ Responsible for tumour surveillance and can induce strong responses to tumours by releasing cytokines ▪ Do not need to recognize a specific antigen to function
 **B lymphocytes (B-cells)**	▪ Produced and mature in the bone marrow ▪ When some B-cells encounter an antigen, they mature into plasma cells (see below) that produce antibodies specific to the antigen ▪ Other B-cells multiply and become memory B-cells that provide long-term memory and protection from a specific threat
 **Plasma cells**	▪ Matured B-cells that recognize antigens and react by producing antibodies ▪ Antibodies attach to antigens on harmful cells and provide a signal for other immune system cells to find and destroy them
 **Dendritic cells**	▪ Activate T-helper cells to stimulate the release of cytokines ▪ Bring/present antigens to other immune system cells so that harmful cells can be easier recognized and destroyed

The immune system and multiple myeloma

What is multiple myeloma (myeloma)?

Myeloma is a cancer associated with the abnormal behaviour of plasma cells, also known as myeloma cells.

The production of normal, healthy plasma cells is a controlled process. When plasma cells age or become damaged, they normally die and new plasma cells take their place. In someone with myeloma, this normal process "breaks down", resulting in the uncontrolled growth of myeloma cells.

Myeloma cells can have a negative effect on different parts of the body and interfere with the production of other types of blood cells by "crowding out" the bone marrow.

Myeloma cells overproduce a type of antibody known as an ***M-protein*** (also referred to as monoclonal protein, paraprotein, myeloma protein or M-spike). Due to the overproduction of myeloma cells and M-protein, several related health problems can occur, some of which are listed here:

- Elevated blood calcium (hypercalcemia)
- Kidney damage
- Low hemoglobin ***(anemia)***
- Bone pain and/or fractures (lesions)
- Frequent or recurring infections
- Fatigue/weakness

The immune system in multiple myeloma

The overproduction of one type of abnormal antibody (M-protein) ultimately results in the suppression of the body's overall immune response. The reduced amounts of healthy antibodies also affect other immune system cells (e.g., T-cells, NK cells, macrophages, etc.) so that they can't perform their usual functions of patrolling and attacking threats.

Myeloma cells have several ways to evade or avoid immune system cells allowing them to multiply and persist. Some of the chemicals (cytokines) they release actually stimulate the growth of myeloma cells instead of triggering an immune response to destroy them. Although their surface can have antigens that make them recognizable as harmful, myeloma cells can develop the ability to stop immune system cells from recognizing and destroying them.

Conventional myeloma therapies

Over the last 60 years, treatment options for myeloma have increased significantly. Despite the development of myeloma immunotherapy, conventional myeloma treatments – corticosteroids, chemotherapy, high-dose therapy and autologous stem cell transplantation, proteasome inhibitors (PIs), and immunomodulatory agents – still play an important role in treating the disease. These conventional treatments are generally used in three- or four-drug combinations – with one of the drugs being a corticosteroid.

Corticosteroids (steroids)

Steroids are chemicals naturally produced by the adrenal gland to help prevent inflammation. Synthetic or man-made steroids most commonly used to treat myeloma are dexamethasone and prednisone.

Side effects of corticosteroids can include:

- mood or emotional changes such as depression, mood swings, agitation, anxiety, or even psychosis;
- fluid retention and swelling, particularly if you also have congestive heart failure;
- increase in blood sugar – of concern to people with diabetes or at risk of developing diabetes;
- high blood pressure;
- difficulty sleeping;
- increased appetite;
- indigestion or heartburn – your doctor may prescribe medication to prevent this side effect;
- hiccups;
- blurred vision – may be short-term (acute) or long-term (if due to cataracts).

Long-term high-dose steroids can result in the development of other side effects, including:

- Cushingoid appearance - weight gain with a “moon face”;
- ***osteoporosis*** or bone loss;
- muscle weakness and/or wasting;
- fatigue and depression.

Chemotherapy

Chemotherapy can reduce the number of myeloma cells in the bone marrow. It does not cure myeloma, but it may stop it from progressing or getting worse for a period of time. *Cyclophosphamide* and *melphalan* are the two most common chemotherapy drugs still used to treat myeloma in Canada.

Chemotherapy is not specifically "targeted" at myeloma cells, it can also damage healthy cells. It destroys cells that divide rapidly (e.g., cancer, hair, skin, blood, intestines) and can lead to side effects such as nausea, loss of appetite, hair loss, mouth sores, diarrhea or constipation, stomach pain, low blood cell counts, and fatigue.

High-dose therapy and autologous stem cell transplantation

In high-dose therapy and autologous stem cell transplantation, "donor" stem cells come from the patient (the recipient). An autologous transplant is the ***standard of care*** and most commonly used therapeutic approach for newly diagnosed transplant-eligible patients with myeloma. The drug used for high-dose therapy is melphalan (chemotherapy).

For more information, please consult Myeloma Canada's *High-dose Therapy and Autologous Stem Cell Transplantation InfoGuide.*

Protein inhibitors (PIs) and immunomodulatory agents

PIs block activity of the proteasome in myeloma cells; this is a mechanism that breaks down proteins that are important for controlling cell division. Blocking the proteasome causes proteins inside myeloma cells to build-up to toxic levels, leading to myeloma cell death.

In Canada, there are currently three PIs available for use in myeloma: *bortezomib* (Velcade), *carfilzomib* (Kyprolis) and *ixazomib* (Ninlaro).

Immunomodulatory agents work against myeloma by:

- directly attacking myeloma cells;
- stimulating or enhancing the effects of immune system cells that identify and fight myeloma cells.

There are three immunomodulatory agents available for the treatment of myeloma in Canada: *thalidomide, lenalidomide* and *pomalidomide* (Pomalyst). The use of thalidomide has decreased due of the availability of lenalidomide and pomalidomide.

Although PIs and immunomodulatory agents do partially enhance immune system cells, they are not considered to be a true form of myeloma immunotherapy.

Some of the more common side effects of PIs or immunomodulatory agents are:

- nausea, vomiting, loss of appetite, diarrhea, constipation, fever, rash;
- lower blood cell counts – i.e., white, red and/or platelets
  - Low white blood cell counts ***(leukopenia)*** can increase your risk of infections like respiratory infection (cold/pneumonia).
  - Low red blood cell counts (anemia) can make you feel weak and tired.
  - Low platelet counts ***(thrombocytopenia)*** can make you bruise easily and increase your risk of bleeding.
- nerve damage leading to numbness, tingling, or pain in the hands and feet (peripheral neuropathy);
- development (re-activation) of shingles (herpes zoster);
- increased risk of blood clots;
- heart problems, kidney or liver failure.

Clinical trials

Please note: At the time of printing, myeloma immunotherapies discussed in this InfoGuide are in development and being investigated in clinical trials.

Clinical trials are research studies done with patients to evaluate new treatments or new ways of combining and administering existing treatments. By testing new drugs or combinations of drugs, each study is designed to find better ways to treat the disease, improve quality of life and answer scientific and clinical questions.

While clinical trials are sometimes the only option available for patients, clinical trials, from Phases I to IV, can also be helpful options for patients throughout their myeloma journey, from ***smouldering multiple myeloma (SMM)***, newly diagnosed myeloma, to ***relapsed or refractory myeloma***.

Often, promising new drugs or combinations of treatments being studied in clinical trials are not yet approved by Health Canada and therefore, unavailable to patients, except through a clinical trial. Clinical trials may also provide access to drugs or combinations of treatments that are approved by Health Canada but are not yet covered by provincial governments.

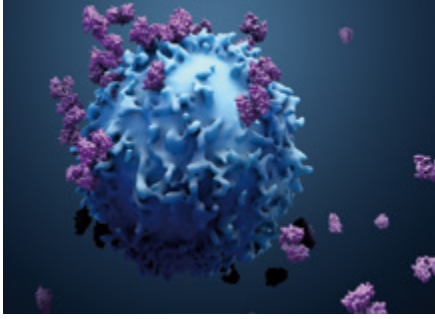
To search for myeloma clinical trials in Canada, visit www.myeloma.ca/findtrials.

For more information on clinical trials or answers to frequently asked questions, please refer to Myeloma Canada's *Clinical Trials as a Treatment Option InfoGuide* by visiting www.myeloma.ca. You may also order a free printed copy by emailing us at contact@myeloma.ca or calling us, toll-free at 1-888-798-5771.

More information

Clinical trials are divided into various steps called phases. As described by the Canadian Cancer Society, here are the most common:

- **Phase I trials** – this is often the first time a new therapy is tested in people. This phase is used to see how safe a treatment is and establish the best dosage. Phase I trials are often offered to people with advanced cancer, or who are no longer responding to treatment, or who have no other treatment options. There are usually 15 to 30 people in a Phase I trial.
- **Phase II trials** – the focus is on how well a treatment works. Throughout this phase, the safety of the treatment and its possible side effects are carefully studied. There are usually fewer than 100 people in a Phase II trial.
- **Phase III trials** – here, a promising new treatment is compared to the standard (or commonly used or accepted) treatment) for a condition or a disease. The intent is to discover if the new treatment is better than the standard one being used. Phase III trials may include people from all over the world and may include anywhere from several hundred to several thousand people.
- **Phase IV trials** - more information is gathered on possible positive and negative effects of the new treatment once it has been approved for use. There are usually several hundred to several thousand people in this phase.



Myeloma immunotherapy: Targeting myeloma cells

Overview

Unlike chemotherapy, myeloma immunotherapy better targets myeloma cells and spares most healthy cells. It can trigger and improve the ability of the cells in your immune system to recognize and destroy myeloma cells.

Because of the way myeloma immunotherapy works in the body, some of the side effects that may occur are different from those seen in conventional myeloma treatments.

Depending on the specific treatment, side effects of myeloma immunotherapy may include, among others:

- infusion- or injection-related reactions:
  - wheezing, trouble breathing, throat tightness, cough, runny/stuffy nose
  - nausea, chills, dizziness/light-headedness, confusion, headache, back pain, weakness, fatigue
  - swelling, itching, rash/hives, and redness at the injection site
- ***cytokine release syndrome (CRS):***
  - fever, nausea, headache, rash, rapid heartbeat, low blood pressure, trouble breathing
- ***immune effector cell-associated neurotoxicity syndrome (ICANS):***
  - partial loss of the ability to speak or write, tremor, lethargy
  - confusion, seizure, loss of consciousness
  - ***cerebral edema***
- other neurologic events:
  - difficulty in understanding
  - loss of balance
- lower blood cell counts (white, red and/or platelets)
- abnormal levels of minerals (e.g., potassium, sodium) in the blood
- other potential side effects specific to the drug used such as temporary vision or skin problems.

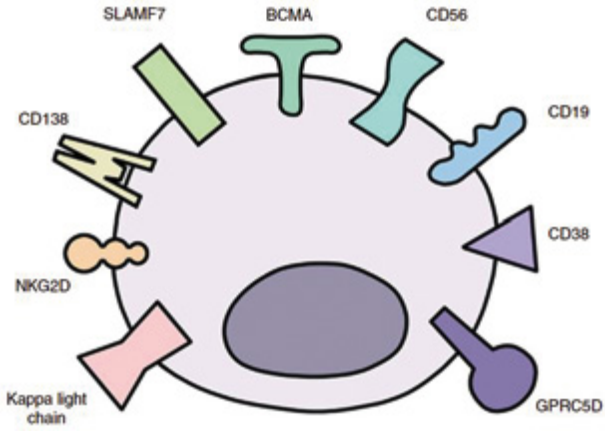
Antigen targets

For myeloma immunotherapy to work at its best, the goal is for the treatment to target antigens that are generally more numerous on the surface of myeloma cells, but not present on most healthy cells. Some antigens may also be on the surface of other cells, so they may not all be possible targets for myeloma immunotherapy.

Many new immunotherapy approaches have been developed to target the B-cell maturation antigen (BCMA) because BCMA is heavily expressed by nearly all myeloma cells but not by healthy plasma cells. There are also specific antigens on the surface of T-cells that could be helpful to "recruit" T-cells and enhance myeloma cell destruction.

Figure 1 illustrates some myeloma cell antigen targets that have been studied or are being investigated (at the time of printing), in clinical trials.

Figure 1 – Myeloma cell antigen targets



Monoclonal antibodies (MoAbs)

MoAbs are one of the most significant advances in immunotherapy. They are laboratory-produced antibodies that recognize specific myeloma antigens. MoAbs also recruit several of your immune system cells to destroy myeloma cells. The term "monoclonal" means that there is one type/clone (identical copy) of antibody.

Two MoAbs have been approved for the treatment of myeloma by Health Canada: *daratumumab* (Darzalex) and *isatuximab* (Sarclisa). Both drugs target the CD38 antigen. *Elotuzumab* (Empliciti) targets the SLAMF7 antigen and is also approved by Health Canada but is not sold in Canada by the manufacturer.

Table 2 – Various MoAbs myeloma immunotherapies in development and being studied in clinical trials

Current clinical trial phase	Name (trade/other names)	Type of MoAb therapy	Antigen target(s)	Method of administration
Phase III	*Belantamab mafodotin* (Blenrep; belamaf; GSK2587916)	Antibody-drug conjugate	BCMA	Infusion
Phase III	*Elranatamab* (PF-06863135)	Bispecific	BCMA & CD3 (on T-cells)	Injection
Phase III	*Teclistamab* (JNJ-64007957)	Bispecific	BCMA & CD3 (on T-cells)	Injection
Phase III	*Talquetamab* (JNJ-64407564)	Bispecific	GPRC5D & CD3	Injection
Phase II	*Pembrolizumab* (Keytruda)	Checkpoint inhibitor	PD-1 receptor (on lymphocytes)	Injection

Note: Only treatments in Phase II or Phase III clinical trials are shown. Treatments in mixed Phase I/II clinical trials are excluded. Information is subject to change. Please visit myeloma.ca/findtrials *for the most current therapies that are in development and available in Canada, or* **ClinicalTrials.gov** *for clinical studies conducted around the world. Last update: August 2022*

The technology used to create MoAbs has been further expanded to include:

- **bispecific MoAbs** – target two antigens one on myeloma cells and one on T-cells to link them together;
- **trispecific MoAbs** – target three antigens one on myeloma cells and two on different types of T-cells to link them together;
- **antibody-drug conjugate (ADC)** – MoAb attached to a drug;
- **antibody-*radionuclide* conjugate** – MoAb attached to a radionuclide;
- ***checkpoint* inhibitors** – designed to target a "checkpoint" on T-cells.

Chimeric antigen receptor (CAR) T-cell therapy

CAR T-cell therapy is typically a one-time treatment that uses T-cells. T-cells are collected from a person's blood by pumping it through a machine that separates the T-cells from the rest of the blood. The collected T-cells are then genetically modified in a lab to express a CAR receptor protein on its surface that can better recognize an antigen on the surface of the myeloma cells to kill them more efficiently.

There are two main types of CAR T-cell therapy:

- **Autologous CAR T-cell therapy**
  - T-cells are taken from the patient, engineered, and infused back into the patient ***intravenously***.
  - With this approach, the manufacturing process can delay the reinfusion of engineered CAR T-cells back into the body.
- **Allogeneic (donor) CAR T-cell therapy**
  - T-cells are taken from a healthy donor, engineered, and infused into the patient intravenously.
  - Allogeneic CAR T-cells may be recognized as being foreign by the patient's body and lead to side effects.
  - This type of approach is considered to be "off-the-shelf" and is not associated with manufacturing delays.

In either autologous or allogeneic CAR T-cell therapy, once the CAR T-cells are infused back into the body, they can multiply and continue to exist, allowing for long-term disease control. Unfortunately, after time, CAR T-cells can also stop multiplying and detecting the myeloma.

A similar type of treatment in development genetically modifies natural killer (NK) cells instead of T-cells (see page 3).

Table 3 – Myeloma CAR T-cell therapies currently in development and being studied in Phase III clinical trials

Current clinical trial phase	Name (trade/other names)	Type of CAR T-cell therapy	Antigen target(s)	Method of administration
Phase III	*Idecabtagene vicleucel* (Abecma; bb2121)	Autologous	BCMA	Infusion
Phase III	*Ciltacabtagene autoleucel* (Carvykti; Cilta-cel; JNJ-68284528)	Autologous	BCMA	Infusion

Note: Only treatments in Phase III clinical trials are shown. Information is subject to change. Please visit myeloma.ca/findtrials *for the most current therapies that are in development and available in Canada, or* **ClinicalTrials.gov** *for clinical studies conducted around the world. Last update: August 2022*

Other immunotherapies

Myeloma vaccines therapies

Vaccines designed for the treatment of myeloma can stimulate the immune system to produce antibodies that can attack specific antigens on the surface of myeloma cells.

Oncolytic virus therapies

Cancer-destroying (oncolytic) viruses can work by directly targeting myeloma cells while sparing healthy cells.

Oncolytic viruses that treat myeloma may:

- infect myeloma cells;
- multiply inside myeloma cells until they burst and release the virus to surrounding areas to infect other myeloma cells and destroy them;
- cause an immune system response against myeloma cells.

Table 4 – Myeloma vaccine and oncolytic virus therapies currently in development and being studied in clinical trials

Current clinical trial phase	Name (trade/other names)	Type of therapy	Method of administration
Phase II	PVX-410	Vaccine (smouldering multiple myeloma)	Injection
Phase I	*Pelareorep* (Reolysin)	Oncolytic virus	Injection
Phase I	TXSVN	Vaccine	Injection
Phase I	SVN53-67/M57-KLH (SurVaxM)	Vaccine	Injection

Note: Information is subject to change. Please visit myeloma.ca/findtrials *for the most current therapies that are in development and available in Canada, or* **ClinicalTrials.gov** *for clinical studies conducted around the world. Last update: August 2022*

Future myeloma immunotherapy research

Over time, several of the treatments discussed in this InfoGuide will be approved for the treatment of myeloma. Myeloma research is constantly evolving and increasing at an incredible rate, Newer, more personalized therapies are being developed that will increase future treatment options for people living with myeloma. Upcoming clinical trials will also evaluate several multi-drug myeloma treatment approaches to determine the best combinations and optimal sequential use.

Additional myeloma treatments in development

Selective Inhibitor of Nuclear Export (SINE)

SINE drugs block the action of protein called exportin 1 (XPO1) in the nucleus (centre) of myeloma cells.

XPO1 is:

- present in high levels in myeloma cells compared to healthy plasma cells;
- important for myeloma cell survival;
- responsible for protecting myeloma cells by moving protein that suppresses tumours to an area inside the cells where they aren't able to reach and kill the myeloma cells.

By blocking XPO1, myeloma cells can undergo a controlled cell death like healthy plasma cells.

Pro-survival inhibitors

Pro-survival proteins normally prevent cells from dying through a regulated process called ***apoptosis*** (also known as programmed cell death). Pro-survival inhibitor drugs can target and block pro-survival proteins (e.g., Bcl-2; Mcl-1) from functioning and thus can speed up myeloma cell death. Bcl-2 and Mcl-1 are found in myeloma cells in higher amounts than in healthy cells. Patients with the mutation t(11;14) have higher levels of Bcl-2 compared to those without the mutation.

Cereblon E3 ligase modulators

Cereblon E3 ligase modulators can cause the breakdown of proteins *Ikaros* and *Aiolos* located inside myeloma cells. Through a series of subsequent events, these drugs can stimulate the immune system to kill myeloma cells.

Table 5 – Additional myeloma treatments in development and being studied in clinical trials

Current clinical trial phase	Name (trade/other names)	Type of therapy	Target(s)	Method of administration
Phase III	*Selinexor* (Xpovio; ATG-010; KPT-330)	Selective Inhibitor of Nuclear Export	XPO1 protein	Oral
Phase III	*Venetoclax* (Venclexta)	Pro-survival inhibitor	Bcl-2 protein	Oral
Phase III	*Iberdomide* (CC-220)	Cereblon E3 ligase modulator	Cereblon	Oral
Phase II	*Mezigdomide* (CC-92480)	Cereblon E3 ligase modulator	Cereblon	Oral

Note: Only treatments in Phase II or Phase III clinical trials are shown. Mixed Phase I/II clinical trials have been excluded. Information is subject to change. Please visit myeloma.ca/findtrials *for the most current therapies that are in development and available in Canada, or* **ClinicalTrials.gov** *for clinical studies conducted around the world. Last update: August 2022*

Beyond family and friends: Myeloma support groups and programs

Local support groups and programs

Talking to people outside your immediate circle may be easier than talking to family and close friends. Meeting and speaking with others with shared experiences can truly provide you with invaluable information and support. Others may be, or have already been, in a similar situation to yours. They understand what you're going through and how to help from a different perspective. Sometimes relief can be found just by speaking to people that can personally identify and relate to you, your experiences and your feelings.

Visit myeloma.ca to find a support group near you. If a physical support group doesn't exist in your area, consider forming one yourself. Myeloma Canada can help you get started.

Virtual, online support groups

You may also be able to meet and connect with others through an online support group. Myeloma Canada has created, and is the lead administrator of many online, virtual patient support groups on Facebook. These closed groups offer a safe environment to connect and exchange experiences with others facing similar challenges. Thanks to the Facebook "translate" button, language barriers can be overcome, enabling you to communicate, in your mother tongue, with people nation-wide. Moreover, the information shared on the page is private and can't be viewed by the public. All members must request to join the group to gain access.

Myeloma peer support

In addition to joining a support group, you may want to talk with someone who has first-hand experience either living with myeloma, or as a caregiver to someone with the disease. Myeloma Canada's *Myeloma Peer Support* program provides you with this opportunity.

You are not alone

Visit myeloma.ca to find a support group near you, learn more about our online Facebook support groups, our peer support programs, and other support resources.

Glossary

Anemia: Decreased blood hemoglobin level. Hemoglobin is found in red blood cells and carries oxygen around the body.

Antibodies (immunoglobulins): Y-shaped protein molecules that have heavy and light chains (portions). Antibodies are produced by plasma cells and attach to and fight infection and disease in the form of antigens (bacteria, viruses, toxins or tumours). Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies disable antigens directly; others make the antigen more vulnerable to destruction by other blood cells.

Antigens: Proteins on the surface of foreign cells or substances that can be recognized by cells of the immune system (leading to the production of protective antibodies).

Apoptosis: A normal cellular process involving a genetically programmed series of events leading to the death of a cell.

Bone marrow: The spongy tissue found inside your bones. It is soft, fatty, and full of blood vessels. Your bone marrow is where most of the blood cells in your body are made.

Cerebral edema: Fluid build-up around the brain that causes increased pressure in the skull (intracranial pressure).

Checkpoint: Immune checkpoints are crucial for regulating the immune system from being too strong. Some cancers can protect themselves through immune checkpoint targets. Blocking the checkpoints with a drug can help T-cells better kill cancer cells.

Clinical trial: A research study done to evaluate new treatments or new ways of combining and administering existing treatments. By testing new drugs or combinations of drugs, clinical trials are designed to find better ways to treat the disease, improve quality, and answer scientific and clinical questions. The overall goal of conducting clinical trials is to improve patient care and outcomes.

Cytokine release syndrome (CRS): A severe and sudden inflammatory syndrome caused by a large, rapid release of cytokines into the blood. CRS can occur after myeloma immunotherapy treatment due to the activation of T-cells.

Immune effector cell-associated neurotoxicity syndrome (ICANS): ICANS is a neurological complication that can occur in the days or weeks following a myeloma immunotherapy treatment that activates T-cells (e.g., CAR T-cell therapy).

Immune response: The way the body defends itself against foreign substances such as bacteria, viruses, toxins, and cancers.

Immune system: The complex group of organs and cells that produce antibodies to defend the body against foreign substances such as bacteria, viruses, toxins, and cancers.

Intravenous: Into/within a vein. Medications (solutions) are administered directly into the vein via an intravenous drip, syringe or catheter (central line) and travel directly to the blood stream.

Leukopenia: A reduced level of white blood cells. White blood cells are important for fighting bacterial infection.

Memory cells: Types of long-lived white blood cells (T-cells and B-cells) that can respond to a particular antigen long after the initial exposure that resulted in their production.

M-protein (monoclonal protein, paraprotein, or M-spike): Also known as myeloma protein. These are antibodies or parts of antibodies found in unusually large amounts in the blood or urine of people with myeloma. M-spike refers to the sharp pattern that occurs on protein electrophoresis when an M-protein is present.

Osteoporosis: Reduction in bone density typically associated with age. The diffuse involvement of bones in a person with myeloma produces what looks like osteoporosis on X-rays and bone density measurements.

Phagocytosis: A process where a phagocyte (type of white blood cell) ingests and destroys a foreign substance (e.g., bacteria).

White blood cells (WBCs) or leukocytes: General term for a variety of cells responsible for fighting invading germs, infection, and allergy-causing agents. These cells begin their development in the bone marrow and then travel to other parts of the body. Types of white blood cells include neutrophils, granulocytes, lymphocytes, and monocytes.

Radionuclide: A radioactive atom or cell nucleus.

Relapsed or refractory myeloma: **Relapsed** disease refers to the reappearance of signs and symptoms of myeloma after a period of improvement or remission. **Refractory** disease refers to myeloma that does not respond to a particular treatment. It may be resistant at the beginning of treatment or become resistant during treatment.

Smouldering multiple myeloma (SMM): Also known as indolent or asymptomatic myeloma. SMM is generally an asymptomatic precursor of myeloma where plasma cells may make up 10%-60% of the bone marrow, serum M-protein is greater than 30 g/L, and urinary M-protein is equal to or greater than 500 mg per 24 hours. However, there is still no anemia, renal failure, hypercalcemia, bone lesions or myeloma-defining events. Because the disease is not yet active, SMM or asymptomatic myeloma is usually observed but not treated until it becomes active.

Standard of care: Treatment (medicine or procedure) or protocol that is accepted and widely used by doctors as an appropriate therapeutic approach for a certain type of disease or condition.

Stem cells: Stem cells (also referred to as progenitor or master cells) are immature cells from which all blood cells develop. A normal stem cell can develop into normal blood components such as red cells, white cells and platelets. Stem cells are found in many of your body's organs, such as the bone marrow. When compared to other kinds of cells in your muscle, nerve or blood, stem cells are unique because they are capable of long-term self-renewal. Stem cells are also unique because they are only partially developed (unspecialized) cells that can develop (or differentiate) into over 200 different types of specialized cells with useful bodily functions (e.g., nerve cells in the brain are able to send messages of pain throughout the body).

Stem cell transplantation: A procedure where blood-forming stem cells are administered intravenously to a patient to replace stem cells that were intentionally destroyed by radiation or high-dose chemotherapy treatment. Patients may receive their own stem cells (**autologous** transplant) or stem cells from a donor (**allogeneic** transplant). An autologous transplant is the standard of care and most commonly used therapeutic approach for newly diagnosed transplant-eligible patients with myeloma. Although called stem cell "transplantation", there is no actual organ removed from a donor to a recipient. Because stem cells were traditionally collected directly from the bone marrow rather than from the circulating blood, the procedure was originally referred to as a bone marrow "transplant".

Thrombocytopenia: Low platelet count that increases the risk of abnormal bleeding and bruising.

Make myeloma matter

Every year, Myeloma Canada provides information to thousands of people impacted by myeloma through programs and services such as InfoSessions, Meet & Greets, the Myeloma Matters online newsletter, webinars, educational and patient journey videos, InfoGuides, and much more.

That's why we need your help. As the only national, charitable organization created by, and for, Canadians impacted by myeloma, we depend on your support and generous donations. Your contribution helps to improve the lives of those affected by myeloma by empowering the community through awareness, education and advocacy programs, and supporting research to find a cure. With your help, we've been making myeloma matter since we were founded in 2005.

Every donation is greatly appreciated and enables us to continue our vital work. There are many options for giving. Whether it's a one-time, pre-arranged monthly, or legacy gift, every donation brings us closer to finding a cure.

Ways you can help

Donate

We invite you to make your donation online at myeloma.ca**,** over the phone by calling toll-free at **1-888-798-5771,** or by mailing a cheque payable to Myeloma Canada:

Myeloma Canada
1255 TransCanada, Suite 160
Dorval, QC H9P 2V4

Fundraise

There are many ways you can support Myeloma Canada, such as taking part in the annual Multiple Myeloma March held in cities across Canada, or by fundraising for Myeloma Canada in your local community. When so much about myeloma is beyond the control of the people that it impacts, fundraising can be a rewarding and fun way of doing something positive for yourself and for others touched by the disease.

Contact Myeloma Canada's fundraising team, toll-free, at 1-888-798-5771 for more information or visit www.myeloma.ca.

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Myeloma Canada publications are extensively reviewed by Myeloma Canada's Patient Advisory Council (PAC) as well as scientific advisors prior to publication. To learn more, please visit www.myeloma.ca.

Sincere thanks to the fundraising efforts of the Canadian myeloma community who make myeloma matter by helping to advance Myeloma Canada's objectives of awareness, education, advocacy, community empowerment and support of clinical research so that a cure may be found.

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