MYELOMA CANADA
MAKING MYELOMA MATTER

InfoSheet

UNDERSTANDING RELAPSED/REFRACTORY MYELOMA

While you may have lived with multiple myeloma for some time, relapse and disease progression remain life threatening and emotionally devastating. That's why exploring your immediate needs with your healthcare team and educating yourself on future treatment options are crucial steps in your myeloma journey. Multiple factors will influence your overall treatment plan when there's no response to treatment (refractory) or the disease comes back (relapse).

Defining the terms *RELAPSED* and *REFRACTORY myeloma*

Relapsed disease:

Relapse is the reappearance of signs and symptoms of myeloma after a period of improvement (at least 60 days after a treatment period). Since relapse is common in myeloma after a remission, you and your healthcare team must think about how to keep your future treatment options as open as possible.

Treatments are able to eliminate most myeloma cells, but they're not able to kill them all. With time, residual myeloma cells can start multiplying and lead to relapse. A person affected by myeloma can experience multiple periods of remission following treatment with consecutive lines of therapy. See below the relapse pattern.

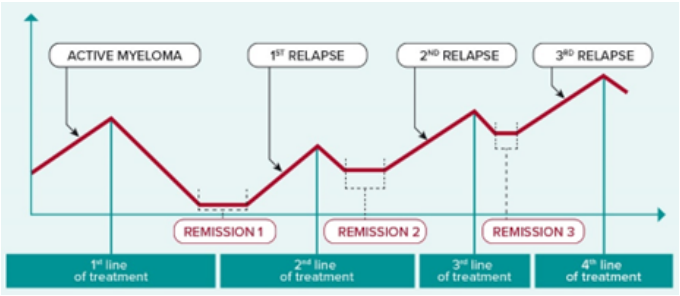


Figure 1: Understanding relapse. web_mc_patient_hanbook_en_2023_final.pdf - Pages (44, 17)

Refractory disease:

Refractory is a relapse with lack of response to treatment. It means that the person affected by myeloma has had a progressive disease during treatment or within 60 days following the start of a new treatment. In cases where periods of remission are short, greater are the chances to experience poor outcomes and have a high-risk myeloma.

Nevertheless, being refractory to a treatment does not mean you are refractory to all treatments. If you develop refractory disease that is no longer responsive to one type of treatment, different treatment options may still be available.

How to detect relapse or find out if you are refractory to treatment?

Reappearance of signs and symptoms can help identify that myeloma has become active again. Your healthcare team will notably monitor any signs of elevated calcium in the blood, renal insufficiency, low levels of hemoglobin in red blood cells (also known as anemia) through regular blood tests. New bone lesions will also be detected on bone imaging tests. It is therefore important to report symptoms such as pain, fatigue, recurrent infections or unintentional weight loss as they can be signs of more severe complications.

More in-depth diagnostic criteria can better identify people who may require active myeloma treatment. These myeloma defining events include the percentage of myeloma cells in the bone marrow, the serum free light chain ratio as well as the number of bone lesions present on imaging (e.g., PET/CT, MRI, X-ray).

Moreover, myeloma cancer cells that are resistant to treatment can be found in people in remission with no symptoms of the disease. Recently, studies have shown that measuring the level of minimal residual disease (MRD) enables faster detection of potential relapses and better adaptation of treatments. To achieve this, the detection of M-protein levels in the blood or bone marrow biopsy can be used to establish MRD. MRD status testing may or may not be available at your cancer centre.

Different treatment options when you relapse

Although the cure for myeloma has not yet been found, novel therapies are enabling individuals to undergo extended periods of remission.

Once relapse occurs, treatment options may include:

- a myeloma drug, usually in combination with a steroid such as dexamethasone
- a second transplant
- new treatments through clinical trials

Treatment is customized to each situation. The initial treatment is called first-line therapy. If there is no response to treatment or if the disease comes back, the next treatment is called second-line therapy. The type of second-line therapy that may be offered to you will depend on what first-line therapy you received and if your myeloma responded to the treatment. For example, if relapse occurs while on lenalidomide maintenance, the myeloma is likely refractory (does not respond) to lenalidomide (e.g., Revlimid) and the myeloma cannot be re-treated with that drug in subsequent lines of therapy. Your healthcare team may then prefer second-line therapy with a drug (i.e., bortezomib [e.g., Velcade]) from a different drug class.

In case of a second relapse, a third-line therapy will be offered. Previously used drugs may be used if the person was not refractory to that treatment. When a third relapse occurs, the fourth-line therapy (and beyond) comes into play. Clinical trials are then strongly considered. There is no standard care in Canada or Worldwide in that case.

Decisions will depend on the following principles:

- Disease factors (response to previous treatments, known high risk disease)
- Patient factors (fitness, frailty and choice)
- Access factors (provincial access, insurance and compassionate access programs)

Other important things to consider with relapse:

- Bone health
- Infection Prophylaxis
- Pain control
- VTE prophylaxis if on blood clots prevention medicine, such as lenalidomide
- Psychosocial care
- Peer support

To get more information on therapies or new and emerging treatments, including immunotherapy, that may be accessible through a trial, please refer to the **Multiple Myeloma Patient Handbook** or the **Myeloma Immunotherapy** InfoGuide available in our resource library at www.myeloma.ca or click here.

Coping with relapse

Experiencing a relapse in your multiple myeloma can be very stressful. You may experience feelings of distress or fear, mixed with hope, as you navigate this stage of the disease, while also exploring new treatment options for now and the future.

Make the most of your healthcare appointments and use the interactive **Discussion guide on psychosocial support for people experiencing a relapse**! This guide has been created to encourage meaningful conversations with your healthcare team about incorporating psychosocial care as a part of your overall treatment plan, and learn about your treatment options. Click here to download a copy and find out more about the different types of psychosocial specialists available to people experiencing a relapse.

You may benefit from support if you are concerned about relapse or becoming refractory to treatment. Find your nearest local support group or use the peer support hotline in the "**Find Support**" section at www.myeloma.ca.

To learn more about relapsed and refractory myeloma, watch our videos at www.youtube.com/@myelomacanada or click here.

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