# Revolutionising Multiple Myeloma Care: Innovative Therapies on the Horizon

Multiple myeloma (MM) is the second most common blood cancer after leukaemia. Over time, the treatment strategies for MM have been changed due to the introduction of many new medications. Conventionally, the treatment involved mostly chemotherapy medications, but now, with the introduction of immunotherapy (which helps the immune system fight cancer), the treatment options are expanding, and patients' survival rates have improved consequently. However, despite all the improvements and progress, MM still can't be cured completely. Although some patients experience significant improvements and can live without signs of the disease for a longer time, a complete cure for MM has yet to be found. This summary talks about the latest progress in treating MM.

## Immunotherapies: the present and the future of MM

The greatest evolution in the treatment of MM is the development of immunotherapies. These have emerged as a milestone in the history of MM treatment, helping patients of all ages and settings (both in the upfront and relapse phases). Given below are the successful immunotherapy treatment options:

### 1. Anti-CD38 monoclonal antibodies

Anti-CD38 monoclonal antibodies (mAbs) have become a key part of treating multiple myeloma (MM), a type of blood cancer. These medications, including daratumumab (the first of its kind) and isatuximab, target a specific protein in the cancer cells and greatly improve treatment for MM patients.

**Early and Advanced Stages:** These therapies are used both at the beginning of treatment (for newly diagnosed patients) and after the cancer has returned or stopped responding to other treatments. They have been shown to be effective in increasing the time patients live without their cancer getting worse and in achieving complete removal of cancer signs in some cases.

**Trials and Studies:** Important studies have shown that combining daratumumab with other cancer medications can significantly help patients, including those who can and cannot undergo bone marrow transplants. Isatuximab is also being tested in similar combinations.

**Benefits for Older Patients:** These medications are especially good for older patients because they cause fewer side effects, making them easier to handle over a long time.

## *"Armed" immunotherapies (CAR-T cells and BsAbs)*

### 2. CAR-T cell therapies

CAR-T cell therapies are a type of treatment that modifies a patient's immune cells (T cells) to recognize better and attack multiple myeloma (MM) cancer cells. These modified T cells are equipped to target a specific protein in the cancer cells called BCMA (B-cell maturation antigen), which is common in MM. The two leading CAR-T cell therapies are idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel). Ide-cel was the first of these to be approved in the US and Europe after showing promising results in a trial, with a significant number of patients responding to the treatment. Cilta-cel also showed very high response rates in its trials.

### 3. Bispecific antibodies

Bispecific antibodies (BsAbs) are a type of cancer treatment designed to help the body's immune system fight multiple myeloma (MM). They work by connecting T cells, a type of immune cell, to the cancer cells, which activates the T cells to attack and kill the cancer cells. Unlike CAR-T cell therapies, which require taking cells from the patient's body, modifying them, and then putting them back, BsAbs are ready-made treatments that can be used straight from the shelf, making them quicker to administer.

### 4. Antibody-drug conjugates (ADCs)

Belantamab mafodotin is an antibody-drug conjugate (ADC), a targeted therapy specifically designed for multiple myeloma (MM) that has become resistant to other treatments. ADCs are made by attaching a powerful cancer-killing medication to an antibody, which helps deliver the medication directly to the cancer cells. This targeted approach aims to minimize side effects by reducing the medication's impact on healthy cells.

### 5. Immunomodulators

Cereblon E3 ligase modulators (CELMoDs) are a new type of medication developed from an older class called IMiDs (thalidomide analogues), used to treat multiple myeloma (MM). CELMoDs work by targeting a protein complex inside cancer cells called cereblon, binding to it more strongly than IMiDs do. This stronger binding leads to the destruction of specific proteins

(IKZF1 and IKZF3) that the cancer cells need to survive. Iberdomide is one of the most studied CELMoDs and has shown promise in treating MM that has returned or resisted other treatments.

## Non-immunological agents

Non-immunological agents are becoming increasingly important in treating multiple myeloma (MM), particularly for patients who have tried most other available treatments. These agents work through new mechanisms or target new aspects of the cancer cells, offering hope where traditional options may no longer be effective. Two notable examples of such novel agents are venetoclax and selinexor.

Venetoclax targets the BCL-2 protein and is particularly effective in MM patients with the t(11;14) translocation, offering the potential for longer disease-free periods but with an increased infection risk. Selinexor inhibits the XPO1 protein, providing a new approach for patients resistant to other treatments despite its side effects, such as nausea and low blood cell counts. These agents represent hopeful advancements in MM treatment, requiring careful management due to their unique benefits and risks.

## Conclusion

The outlook for multiple myeloma (MM) treatment is promising due to advances in immunological therapies, such as anti-CD38 antibodies like daratumumab and isatuximab, which are key for various MM stages, including smouldering MM (benign stage of myeloma without any symptoms). Emerging treatments like CAR-T cell therapies and bispecific antibodies are offering new hope, particularly for relapsed MM. The development of non-immunological therapies targeting specific genetic markers, like venetoclax, marks a move towards personalized treatment. As research continues, the goal is to improve treatment options and work towards a cure for MM.