



# Myeloma and the Immune System

- Myeloma is a cancer of the immune system cells (plasma cells) that make antibodies to help fight infection.
- When even one part of the immune system is affected, the whole system suffers.
- Myeloma suppresses the immune system as a whole, reducing the number of normal antibodies and affecting all the cells that patrol for and attack abnormal cells.
- Successful treatment brings with it recovery of the immune system.

## What are the key immune system cells?

- The immune system has two major components: the innate response, made up of cellular proteins and killer cells, and the adaptive response, based on the ability of immune system cells to recognize and attach to specific antigens on the surface of infected cells and tumor cells.
- The immune system is made up of white blood cells that circulate in the bloodstream and the lymphatic system.
- Lymphocytes (B cells and T cells) are the white blood cells responsible for the adaptive immune response.
- Natural killer (NK) cells are responsible for tumor surveillance. They can recognize and kill infected cells without recognition of specific antigens.

## Using the immune system in myeloma

- Immuno-oncology is the treatment of cancer with therapies that trigger cells in the immune system.
- Immunotherapies can help restore the immune system's ability to find and fight cancer cells.
- Many types of therapies that are already approved for myeloma have immune system effects, and other immunotherapies are in clinical trials for myeloma.

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## Approved immunotherapies

**Darzalex® (daratumumab):** An anti-CD38 monoclonal antibody that targets and attaches to a specific antigen (CD38) on the surface of myeloma cells and then signals NK cells to attack and kill them. While it is effective as a single agent, it is even more effective as part of FDA-approved combination therapies.

**Empliciti® (elotuzumab):** An engineered anti-SLAMF7 monoclonal antibody that attaches to NK cells and then stimulates the NK cells to attach to and attack myeloma cells via a SLAMF7 receptor. This type of antibody is effective in combination with other myeloma therapies.

## Promising clinical trials

**Monoclonal antibodies** targeting various myeloma cell surface antigens are being investigated in numerous clinical trials.

**Antibody-drug conjugate (ADC),** an anti-cancer therapy that links a monoclonal antibody directed at myeloma cells with a drug (cytotoxic agent) that is toxic to cancer cells. The ADC binds to specific receptors on the surface of the cancer cells, then the linked drug enters the cancer cells and kills them.

**Bispecific T-cell Engager (BiTE),** an artificial monoclonal antibody designed for use as an anti-cancer drug, simultaneously attaches to a cell surface antigen on cancer cells and to a receptor on cytotoxic (cell-killing) T cells. This dual binding brings cytotoxic T cells in close range to cancer cells to kill them. BiTEs currently in clinical trials for myeloma attach either to B-cell maturation antigen (BCMA) or to GPRC5D on the surface of myeloma cells, and to CD3 on T cells.

**Chimeric antigen receptor (CAR) T-cell therapy** is a technique in which a patient's T cells are collected and genetically engineered to attack the patient's tumor cells. Investigators are testing new approaches to increase the efficacy and reduce the toxicity of T-cell therapy.

***As always, the IMF urges you to discuss all medical issues with your doctor, and to contact the IMF with your myeloma questions and concerns.***

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