

# Immune Cell Regeneration and Gaining Strength to Attack Multiple Myeloma Cancer

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## ABSTRACT

Multiple Myeloma is a rare cancer that primarily affects plasma cells that differentiate into white blood cells (which have important roles in the immune system such as fighting off infections and diseases). Once these plasma cells are transformed into cancerous cells that invade the space of the bone marrow, there is a prevention of the existence of future healthy immune cells that help the human body systems. Due to these viscous effects of the Multiple Myeloma, the blood cell count decreases and patients' immunity lowers. The weakened immune systems of patients can attack the components of the treatments which leads to the wastage of money, time, and energy of the patients and the medical professionals. With the current research, patients can gain back strength and improve their immune systems. By the usage of the regeneration of stem cells, immunotherapy to increase the resistance of immune cells against the cancer, Chimeric Antigen Receptor T Cell therapy (or CAR-T Cell Therapy), and monoclonal antibody therapies, patients can gain back strength and improve their immune systems in a way that attacks Multiple Myeloma. Yet there is still growth for improvement, since the process of patients receiving treatments must be repeated multiple times due to the intensity and persistence of this cancer. By studying and researching the effects of Multiple Myeloma on immune cells, this paper's goal is to find ways to improve current treatments and how to regenerate stronger and healthier immune cells which can resist and potentially defeat Multiple Myeloma Cancer.

## Introduction

Millions of cancer patients are prone to illnesses because cancer cells can enter the patients' bone marrow, a source that produces red and white blood cells, and destroys the ability of producing healthy cells. The immune system is an essential part of life due to its ability to protect the body from dangerous invaders, including bacteria and diseases. When Multiple Myeloma attacks a patient with an unhealthy immune system that lacks the necessary amount of white blood cells, they will be more likely to suffer. In the United States alone, around 0.76% of people, mainly over the age of 60, have the risk of having this cancer (American Cancer Society, 2023; Howlader et. al., 2017; National Cancer Institute, 2018). Luckily, with the rise of modern-day research and technology, more cancer treatments and medicines are being discovered and used. But even with these great solutions which have produced successes, the process of performing these treatments is repeated multiple times due to the persistence, intensity, and continuous mutations of Multiple Myeloma. Without solving this root problem with a method in which Multiple Myeloma cancer cells are somehow prevented from attacking healthy plasma cells and the bone marrow, a cure to this cancer may not be found any time soon. Continuous creations of treatments can't solve this situation, rather creating a strategy that resists and targets these cancerous cells (including their mutant variations) will lead to better results. By taking advantage of the capabilities of immunotherapy and building up on current successful mechanisms that only need to be taken once or a few times, the immune system of cancer patients across the globe can be strengthened enough to attack cancer. Understanding

the main problem, and the relationship between Multiple Myeloma and functions of the immune system will allow higher chances of survival and success rates of cancer treatments.

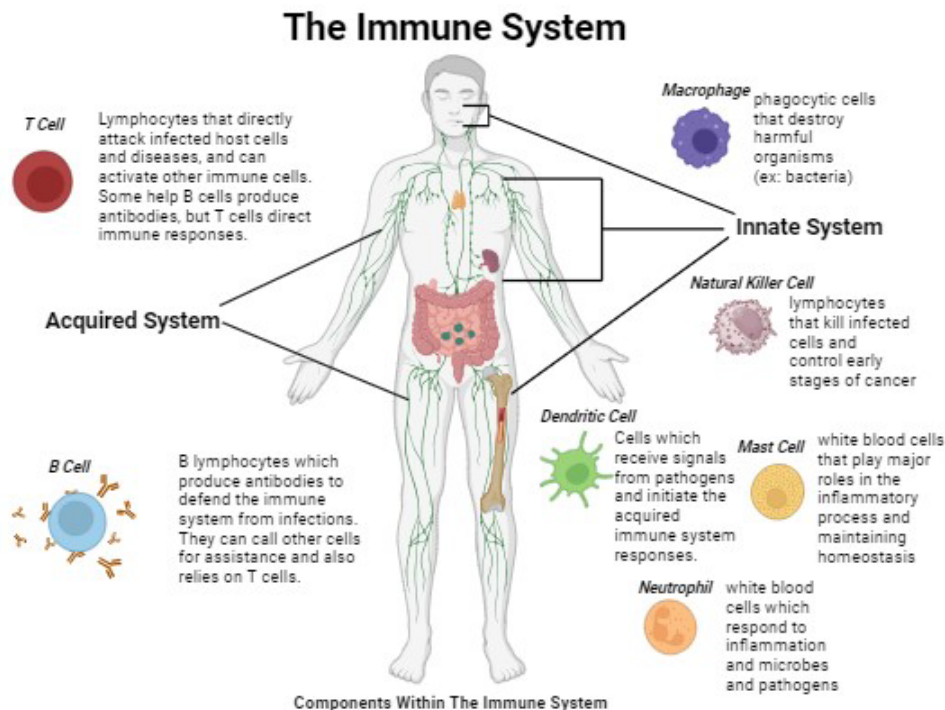
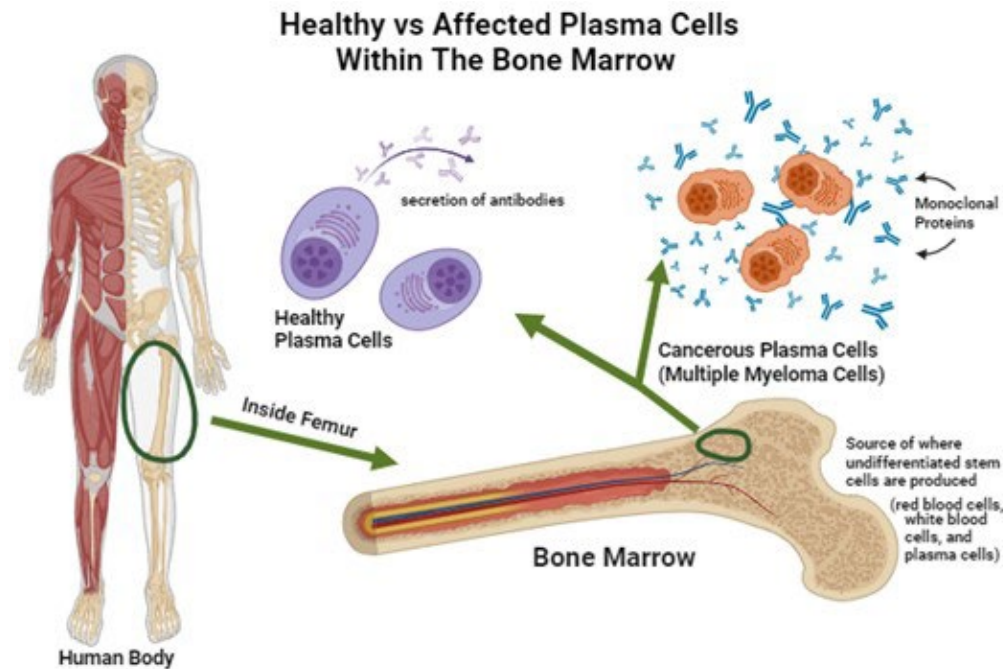


Figure 1. Diagram of the immune system and its cellular components. Created with BioRender.com

## The Immune System and Cancer

The immune system is a vital part of life due to its ability to protect the body from dangerous invaders, including bacteria and diseases. There are two main parts of this system that work with one another: innate immune system and acquired immune systems. The innate immune system is known as the first line of defense. It is the first barrier harmful germs, cells, or parasites encounter when entering the human body. These barriers include the respiratory system, skin, eyes, and much more. Cells such as macrophages, neutrophils, natural killer cells, and phagocytes cooperate with one another to defeat these invaders. If the innate system isn't capable of defeating the invader, then the acquired immune system activates. This part of the immune system contains B cells which make unique antibodies to fight against specific invaders. Memory cells also play an important role in the acquired system since after the first exposure these cells will be able to adapt and destroy them repeatedly later on. Several other components, like T-cells, which clean up dead tissues and attack cancerous cells, all work together to accomplish the main goal, maintaining a healthy human body (National Library of Medicine, 2020). But dangerous diseases such as myeloma cancer can weaken the immune system leaving the human body vulnerable to common illnesses causing serious harm. Cancer cells divide excessively by creating their own growth factors which leads to tumors and the malfunctioning of the body. These cells can enter bone marrow, where blood cells are made, and deplete space and nutrient sources for bone marrow cells. This leaves the immune system with few cells that are sufficient to fight infections. Cancer treatments are used to fight off cancer, but certain procedures, such as chemotherapy which specifically targets fast dividing cells including hair follicles, can injure cells in the skin or cause damage to the skin or mucous membranes. The damaging of

these membranes allows far more dangerous infections to enter the body and due to this instead of chemotherapy, immunotherapy is best suited. Although it does depend on the patient and their reaction to the treatment. Immunotherapy, which doesn't damage cells that aren't meant to be targeted, helps the patient regain their immune system's capabilities (McCluskey, K., 2022). With the help of specific procedures, the immune system can gain the ability to detect and destroy cancerous cells.

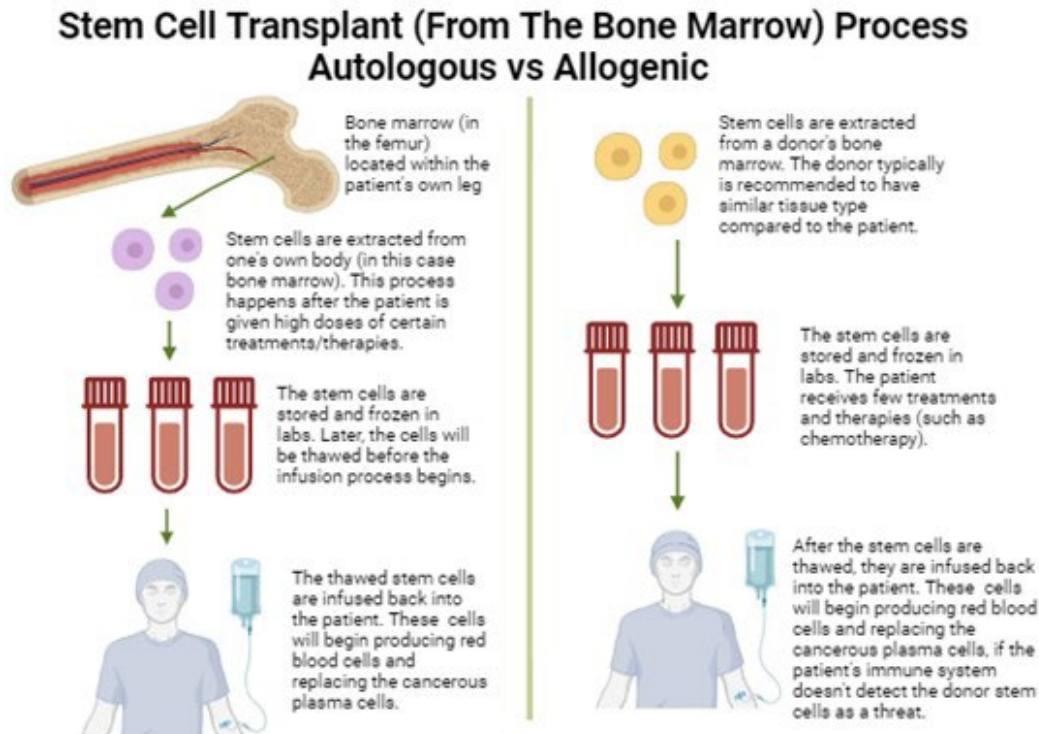


**Figure 2.** The diagram above is a representation of the difference between plasma cells that have and have not been affected by Multiple Myeloma within bone marrow. Created with BioRender.com

## Multiple Myeloma

Multiple Myeloma is the second most common blood cancer and each year over 30,000 new patients are diagnosed with this (American Cancer Society, 2023). This cancer turns plasma cells cancerous and malignant, resulting in the prevention of the bone marrow's ability of producing normal cells. Plasma cells that are eventually differentiated white blood cells, can produce antibodies to help fight as part of the immune system (Professional, C. C. M., 2022). Multiple myeloma cancer cells contain monoclonal proteins on their surface. The monoclonal proteins don't have the ability to fight infections, but rather they take up space and prevent the production of red blood cells, white blood cells, and platelets from being created. This causes impaired immunity, damage to bones and the kidney, and high viscosity of blood. Multiple myeloma is diagnosed after several tests that examine bone marrow, viscosity of blood, number of blood cells, and urine. A good indicator of this disease is the detection of monoclonal proteins within blood samples (Leukemia & Lymphoma Society, 2013). Not only does this cause serious impacts to the body and invade the bone marrow of space, but also negatively affects the immune system. Because there exists the prevention of growth of undifferentiated stem cells within the bone marrow, new healthy white blood cells aren't produced. Causing a lowered supply of immune cells.

This also results in the patient's inability to detect and attack diseases, infections, and illnesses (American Cancer Society, 2020). Which explains why Multiple Myeloma cancer patients experience extreme fatigue and several organ failures. Fortunately, the revival of the immune system functioning is possible with the help of stem cell culture treatments.



**Figure 3.** Diagram of the process of autologous and allogeneic stem cell transplants for patients suffering with cancer. Created with BioRender.com

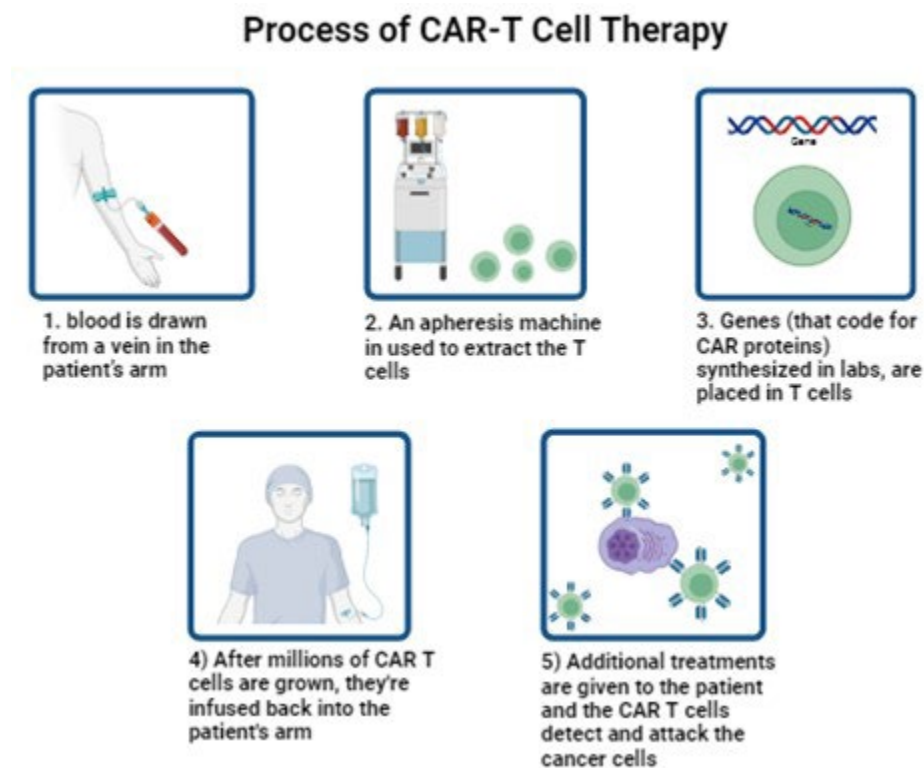
## Stem Cell Regeneration and Its Process

Stem cells are undifferentiated cells that can replicate and transform into specialized cells under certain conditions (Dulak, J. et. al., 2015). These cells are made within the bone marrow, a spongy layer inside a bone, and have the potential to transform into red blood cells, white blood cells, and platelets. Typically, stem cell transplants are used for replacing destroyed cells caused by cancer or by cancer treatments (Cancer Research UK, 2022). The transplant can be allogeneic, meaning the source of the stem cells are from someone other than the patient, but it is possible for your body's immune system to detect the transplanted differentiated cells as foreign. This causes white blood cells to attack the transferred stem cells and further weaken the patient. This is a severe case that is also known as the graft-versus-host disease. Due to this problem, several tests must be performed on the patient and the donor's stem cells should be quite similar compared to the patient's stem cells. Once these tests and diagnostics of the patient's general health are completed, the success rate of the treatment increases. Another option would be an autologous transplant, meaning the source of the stem cells is from the patient (National Cancer Institute, 2015). Even if the transplant is successful, the myeloma cancer won't be fully cured. An even larger problem remains, which is after the procedure, Multiple Myeloma still can overtake the patient. Cancerous cells can attack the recently regenerated cells. Since this cancer causes harm to the bone marrow source, how will the stem cells (that are used in autologous transplants) be produced in the first place?

This results in the same position as before and eventually leads to an even weaker immune system due to the excessive and unbeneficial expenditure of the patient's energy. Thus, there must be a treatment which regenerates stem cells and specializes it into a strong healthy immune cell that will be able to resist and attack the cancer.

## Immunotherapy

Immunotherapy is a great treatment that enhances the patient's body's functions and can either activate stronger immune responses or help the immune system destroy cancer cells. Unlike chemotherapy, immunotherapies are specified to target one type of cancer which is beneficial since it doesn't harm healthy cells. Depending on the patient, side effects can vary. Common side effects - not for all people - are diarrhea, itchiness, rashes, and flu-like symptoms (National Cancer Institute, 2023). Immunotherapy allows the immune system to detect specified cancer cells' proteins that would typically seem normal to the average untreated immune system. This would allow the immune system to strengthen, which would higher the chance of success of the treatment, and attack Multiple Myeloma. Immunotherapy comes with a variety of treatment options, such as T-Cell Transfer Therapy and Monoclonal Antibody Therapy (National Cancer Institute, 2019). These are specifically designed to attack blood cancers, such as Multiple Myeloma Cancer.

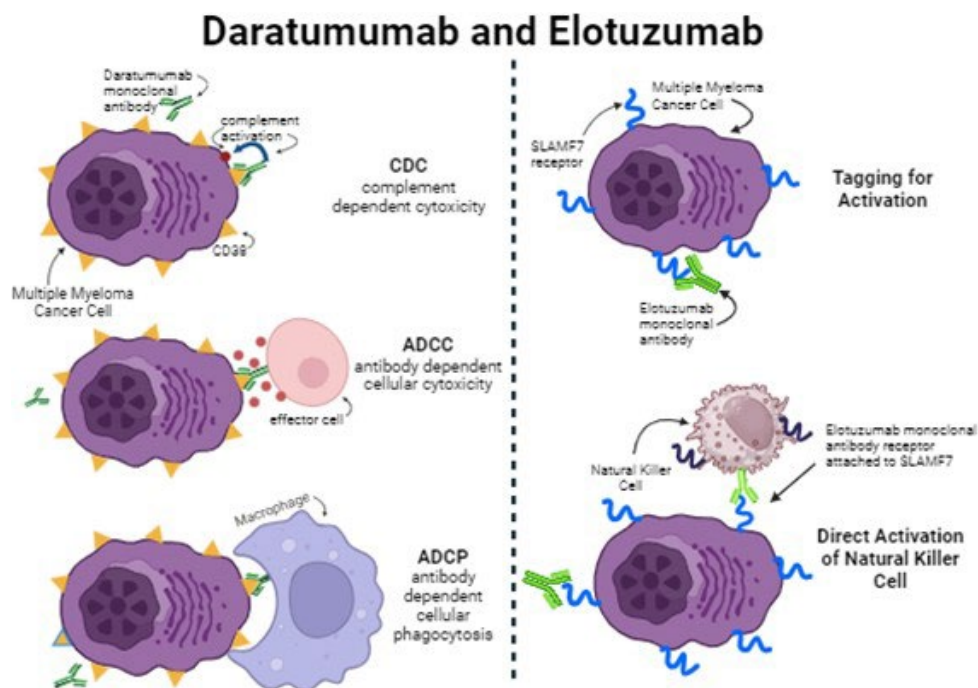


**Figure 4.** Diagram showing the process of CAR – T Cell Therapy. Created with BioRender.com

## CAR – T Cell Therapy

CAR-T Cell Therapy is an immunotherapy which uses a patient's T cells and genetically alters it to have the ability to attack cancer, in this case Multiple Myeloma. T cells have receptors which detect antigens, molecules

that generate antibodies. These antigen receptors are genetically modified in labs to find and destroy specific cancerous cells with complementary antigens. The treatment is performed by first drawing blood from a vein in the patient's arm and using an apheresis machine to separate the T cells. Next, scientists synthesize and multiply proteins called CAR (chimeric antigen receptors). The CAR proteins allow the T cell to recognize and bind to specific proteins / antigens found on the surface of cancer cells. Once the CARs are placed in the genes of the T cell, the T cells are which eventually is injected back into the arm. Other additional medicines and treatments, such as chemotherapy, are used to increase effectiveness. Side effects of this treatment are related to flu like symptoms, cytokine release syndrome and neurological effects (National Cancer Institute, 2022). CAR – T Cell Therapy also has restrictions with its ability to treat solid tumors and its persistence in fighting against reoccurring cancers (Stern, R. C. & Stern, R. M., 2021). Ideally the patient would have healthy bone marrow, but what if a patient were to have a low T cell (or blood cell count in general), the question about how CAR – T Cell Therapy can be performed with a lack of T cells arises. For patients in the later stages of Multiple Myeloma, there are far more complications related with the insufficient amount of stem cells (that would have differentiated into T cells) and unhealthy bone marrow. Luckily, allogenic stem cell transplants are a possible and excellent option to tackle this problem. Another possible source of stem cells for these could be from donated cord blood, but more research is needed to support and raise the chances of success for these (WebMD, 2017). Although stem cell transplants are great solutions, it is still possible that patients with weakened immune system may attack the transplants they received from donors. This proves that in the near future, experiments and research should be conducted to build off and improve current treatments that have the potential to be successful.



**Figure 5.** Diagram of two Monoclonal Antibodies used for therapies to treat Multiple Myeloma Cancer. Created with BioRender.com

## Monoclonal Antibodies

Monoclonal Antibody Therapy is an immunotherapy which uses synthesized antibodies that can attach to specific proteins of the cancer cells' surface, and eventually prevent the metastasis of the cancer. Monoclonal antibodies, which are different from the harmful monoclonal proteins or m spike, can block the Multiple Myeloma growth, flag the cancerous cells to showcase to immune cells to attack the cancer, or input harmful substances to the cancerous cells (National Cancer Institute, 2019). Daratumumab is a monoclonal antibody cancer drug that specifically targets CD38, also known as cyclic ADP ribose hydrolase, which is a protein found commonly found on myeloma cells. This allows the immune system to recognize and attack the cancerous cells. When Daratumumab is crosslinked, this causes the apoptosis of Multiple Myeloma cells (Atanackovic, 2016). Another monoclonal antibody cancer drug is Elotuzumab. When Elotuzumab is combined with other drugs, this leads to promising results in the attack against Multiple Myeloma. Elotuzumab targets SLAMF7, which is a cell surface receptor heavily expressed on cancerous cells. The drug binds to SLAMF7 of the Multiple Myeloma cells. This cancer drug attacks the cancer cells without harming other similar members of the SLAM family (for example, Natural Killer Cells). Since SLAMF7 receptors are also found on the surface of Natural Killer cells; they will be impacted by Elotuzumab (Magen & Muchtar, 2016). Rather than damaging other autologous natural killer cells, this cancer drug activates those cells, which causes myeloma cell death (Balasa et al., 2014). Due to the discoveries and continued research of immunotherapy drugs - such as Daratumumab and Elotuzumab - frequently taken treatments to fight against Multiple Myeloma have been successful, not only to attack the cancer but also to boost the patients' immune systems. Monoclonal Antibody Therapies are great treatments, but with a technique that allows scientists to find ways to boost these cancer drugs' ability to detect mutant versions of the cancerous cells, then there is an increase in the potential to defeat Multiple Myeloma.

## Conclusion

Although the battle against Multiple Myeloma still continues to this day, several promising treatments have led to the bettering of many patients and their immune systems. Solely performing stem cell transplants creates the issue of endless cycles of wasting energy and health. But by combining multiple treatments and solutions, there are higher chances of success rates of effectiveness of these procedures. After the patient receives immunotherapies (which is essential to boost immunity), then stem cell transplants can occur. This allows there to be a more likely successful replacement of any damaged immune cells and also prepares the patient to better face relapse periods. But because there are numerous complications for each patient's body, it can be suggested that improvement on immunotherapies (including CAR – T Cell Therapy and Monoclonal Antibodies). Improvements include finding ways to enhance these treatments' capabilities by increasing the immunity of patients' serious conditions near the further stages of Multiple Myeloma, that suffer with the lack in availability of stem cells within the damaged bone marrow, meanwhile not inflicting harm on the patient's body systems. Another recommendation is increased research on finding other methods to make transplant of stem cells (which will be able to differentiate into white blood cells) much more effective and safer, in such a way that the patient won't be able to reject the given treatment. This must be discovered in order to defeat this cancer. With advancements on current successful medications and immunotherapies, the boosted immune system of patients can increase their overall health, esteem, and reaction to treatments, meanwhile decreasing the effects of Multiple Myeloma.

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