Exploring the Use of Immunotherapy Techniques in Lymphocytic Leukemia

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Exploring the intricate encounter between our immune system and Lymphocytic Leukemia reveals how our immune system play a pivotal role in combating cancer, highlighting the importance of immunology in deciphering and overcoming this complex disease.

Details of Lymphocytic Leukemia

Lymphocytic Leukemia is a type of cancer that affects white blood cells and these White Blood Cells cause blockage and can crowd out healthy blood cells choking the bloodstream. Although the exact cause of Leukemia is not known, scientists believe that it may be because of factors like genetics, lifestyle, and environmental exposures. There are two different types of Lymphocytic Leukemia: Acute Lymphocytic Leukemia and Chronic Lymphocytic Leukemia. Acute Lymphocytic Leukemia affects mostly children and younger adults and Chronic Lymphocytic Leukemia affects mostly older adults but there can be exceptions. Lymphocytic Leukemia, like most cancers, manifests more in the developed parts of the world, mainly in North America and Europe. There are many underlying mutations to Lymphocytic Leukemia such as the Philadelphia Chromosome which is a translocation between chromosomes number 9 and 22, BCR-ABL1 *fusion gene* which causes the cancerous cells to have abnormal Tyrosine Kinase activity, TP53 which causes the cells to have a certain resistance to therapy, and NOTCH1 which allows the cell to proliferate and differentiate. Acute Lymphocytic Leukemia needs to have expedited treatment which makes it have a lower life expectancy while people with Chronic Lymphocytic Leukemia inhabit a patient for decades with treatment taken sporadically and controllably. Some forms of treatment are Chemotherapy, Radiation, Immunotherapy, and stem cell transplantation. Getting Chronic Lymphocytic Leukemia is a very small chance almost .57% or 1 in every 175 people in the United States of America. This risk is minutely more for men. For Acute Lymphocytic Leukemia, the percentage to get it is even smaller at about less than 1% of all cancer cases in the United States of America. Even though mostly children get Acute Lymphocytic Leukemia, most deaths occur with adults with 4 out of 5 deaths occurring with adults.

Immunology Methods to Prevent and Hinder Lymphocytic Leukemia

Scientists use both immune checkpoint inhibitors and Chimeric Antigen Receptors (CAR) T cell therapy to treat Lymphocytic and Lymphocytic Leukemias. Immune checkpoint inhibitors target pathways like PD-1/PD-L1 and CTLA-4 to enhance and utilize T cell responses against Leukemia cells. Chimeric Antigen Receptors (CAR) T cell therapy genetically modified the patient's own T cells to recognize and destroy cancer cells.

A substantial way for Leukemia cells to avoid T cells from recognizing them is to overregulate and overexpress the molecule PD-L1 to confuse and hinder T cells. When PD-L1 on a somatic cell attaches to PD-1 on a T cell this causes the T cell to deactivate and eliminate the somatic cell. This prevents T cells from activating and makes them go through Apoptosis, (this process makes the T cells break down). Immunotherapy techniques are then used to hinder this interaction between PD-L1 and PD-1, causing the T cell work and destroying the Leukemia cells. This is how Immune Checkpoint Inhibitors block the T cells from going through Apoptosis.

Then there is CAR T cell therapy which is when scientists draw out blood from patients, separate the T cells from the blood and then they modify the T cells to locate special proteins on the surface of Leukemia cells. Then they infuse the T cells back into the patient's blood and the newly modified T cells fight for the patient against the cancer they were altered for. CAR T cell therapy has shown incredible success but it is incredibly expensive as it is personally tailored to one patient only. This means the entire process has to be done many times by only specialized scientists for each patient.

For (CAR) T cell therapy the number ranges from as low as 30% to 40% (Blood Advances 2023) with different T cell changes having different ranges. A major limitation to these forms of treatments are that they are very expensive with (CAR) T cell therapy being incredibly hard to afford for most patients. There are also many side effects with these treatments like Cytokine Release Syndrome (Cough like symptoms or even low blood pressure and organ dysfunction), Neurotoxicity (Confusion, delirium, and nausea), and the fact that (CAR) T cell therapy does not work on solid tumors. Some problems with these techniques are that (CAR) T cell therapy may inadvertently kill innocuous somatic blood cells if programmed improperly and that the cancer cell can always relapse and come back. (CAR) T cell therapy has been approved by the FDA for the treatment of B-Cell Acute Lymphoblastic Leukemia using drugs like Blinatumomab, Nelarabine, and Inotuzumab ozogamicin which is a form of Acute Lymphocytic Leukemia. There are also many drugs for Immune Checkpoint Inhibitors like Nivolumab, Pembrolizumab, and Cemiphlimab.

Research and Studies on Immunology TReatments for Leukemia

There was a study in 2019 in Seoul, South Korea for Lymphostatic Leukemia, with it more particularly referencing the recurrence around the marrow. They are using the drug, Idarubicin for the reinduction stage and they use Blincyto for the study. This study is in stage 2, with more various human trials and with people more at risk for any more cancer progression. They took anyone who is at least more than one years old and at most 22 years old. The patients could not have received Blinatumomab before this study either. The study focused on many exclusion factors such as patients should also have adequate renal function, could not have the Philadelphia chromosome, could not have any mixed phenotypes for leukemia, could not have had HIV either. Patients would be tested with Blinatumomab and then the efficacy rate, disease free survival rate, and the death rate related to treatment would be tested. The patients would be tested for an average of 9 years.

A recent Phase II clinical trial by Amgen Research (Munich) GmbH investigated the use of Blinatumomab (MT103) in targeting minimal residual disease of B-precursor Acute Lymphoblastic Leukemia (ALL).The scientists used Blinatumomab to treat patients with Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL). Blinatumomab doesn't directly repair the Philadelphia Chromosome, but it can help eliminate leukemia cells that carry this abnormality. The inclusion criteria they used is that the patients must have B-precursor ALL and complete hematological remission with molecular failure, must also be able to sign their informed consent to do so. Some of the exclusion criteria is that they do not have a history or have a current autoimmune disease, cannot have any anti-murine antibodies, cannot be pregnant or nursing either, cannot have any current extra medular involvement.

Citations

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