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**The Effect of CAR-T Cell Therapy in The Treatment of Cancer,
And Associated Side Effects**

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- **Date of submission:** 14/4/2018

Abstract:

CAR-T Cell immunotherapy is an adoptive cell immunotherapy in which t-cells are reprogrammed to attack cancer cells through a specific surface antigen. It's thought to be very effective, but side effects should also be considered.

In this paper, three reports that study the effect of CAR-T Cell therapy on certain types of cancer, and associated side effects is discussed.

Introduction:

When the immune system is functioning normally, immune cells move around the body looking for things that don't belong, like bacteria and viruses. These immune cells search for invaders using "receptors". When receptors find invaders in the body, special immune cells come in to destroy them; these cells are called cytotoxic T cells.

Unfortunately, cancer cells are often able to hide from immune cells, which is why the cancer cells can grow out of control. Immunotherapy is a cancer treatment intended to make the body's immune system able to detect and destroy cancer cells. Immune checkpoint inhibitors have been a successful immunotherapy approach because it pushes the immune system into high gear to fight cancer.

CAR T-cell therapy, however, is different. It is a type of immunotherapy called "adoptive cell immunotherapy."

In CAR T-cell therapy, a person's T cells are removed and taken to a laboratory. The T cells are genetically changed so they will attack cancer cells. These CAR T cells are grown in large numbers and then injected into the patient. One of the remarkable things about this treatment is that it is a "living therapy." CAR T cells typically have to be injected only once, because they go on to multiply in the body. CAR T cells continue fighting the cancer in the patient's body, and their effectiveness may even grow over time.

This new cancer treatment approach is powerful and does come with serious risks that need to be considered before starting therapy. In particular, possible side effects include cytokine release syndrome (CRS) and neurologic problems.¹

Discussion:

1- Chimeric Antigen Receptor T Cells In Refractory B-Cell Lymphomas:

A study involved 28 adult patient with diffuse large B-cell lymphoma or follicular lymphoma that had relapsed or was refractory to previous treatments. Autologous T cells that express a CD19-directed CAR (CTL019) were used. Patients were monitored for response to treatment, toxic effects, the expansion and persistence of CTL019 cells in vivo, and immune recovery. 18 of 28 had a response (64%). Complete remission occurred in 6 of 14 patients with diffuse large B-cell lymphoma (43%) and 10 of 14 patients with follicular lymphoma (71%). CTL019 cells proliferated in vivo and were detectable in the

blood and bone marrow of patients who had a response and patients who did not have a response. Sustained remissions were achieved, and at a median follow-up of 28.6 months, 86% of patients with diffuse large B-cell lymphoma who had a response and 89% of patients with follicular lymphoma who had a response had maintained the response. All patients in complete remission by 6 months remained in remission at 7.7 to 37.9 months (median, 29.3 months) after induction, with a sustained reappearance of B cells in 8 of 16 patients and with improvement in levels of IgG in 4 of 10 patients and of IgM in 6 of 10 patients at 6 months or later and in levels of IgA in 3 of 10 patients at 18 months or later.²

2- CAR T-Cell Therapy Sends Multiple Myeloma Into Remission.

Another clinical trial involved 35 patients with either relapsed or refractory **multiple myeloma**. Of those 35, 33 patients (94%) had a remission within 2 months of receiving the CAR T cells. So far, the researchers have been tracking the health of 19 of those patients for more than 4 months, and among them, 14 have experienced a complete remission, meaning the cancer cannot be detected in the body and there are no symptoms, and 5 had a partial remission. Only 1 patient had the cancer grow worse after treatment, and that patient first had a partial remission for 3 months. There are 5 patients who have been monitored by researchers for 12 to 14 months so far, and all have no detectable cancer cells in their bone marrow.

Cytokine releasing syndrome occurred in 85% of the patients, but it was temporary and most patients had mild and manageable symptoms. No patients had neurologic side effects.³

3- Long-Term Follow-Up Of CD19 CAR Therapy In Acute Lymphoblastic Leukemia.

Another study involving 53 adults with relapsed **B-cell Acute Lymphocytic Leukemia** (ALL) who received an infusion of autologous T cells expressing the 19-28z CAR at the Memorial Sloan Kettering Cancer Center (MSKCC). Safety and long-term outcomes were assessed, as were their associations with demographic, clinical, and disease characteristics.

After infusion, severe cytokine release syndrome occurred in 14 of 53 patients (26%), & 1 patient died. Complete remission was observed in 83% of the patients. Patients with a low disease burden (<5% bone marrow blasts) before treatment had markedly enhanced remission duration and survival. Patients with a higher burden of disease (\geq 5% bone marrow blasts or extramedullary disease) had a greater incidence of the cytokine release syndrome and neurotoxic events and shorter long-term survival than did patients with a low disease burden.⁴

Conclusion:

- CAR T-cell therapy can be effective in the treatment of Acute lymphoblastic leukemia, multiple myeloma, diffuse large B-cell lymphoma, follicular lymphoma, with a recovery of B cells and immunoglobulins in some patients.
- Risks associated with CAR T-cell therapy are substantial, leading to ICU-level care in some cases, but is mostly mitigated; these include: encephalopathies, and cytokine releasing syndrome, with markedly lower incidence among patients with low disease burden.

Recommendation:

It is important for more pediatric and adult patients to be enrolled in clinical trials. Larger study samples, evaluated over more extended periods, will help researchers further understand the impact of this type of therapy, ways to reduce its toxicity and improve the management of adverse side effects.

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