Survivorship Considerations After CAR T-Cell Therapy

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As more patients receive treatment with chimeric antigen receptor (CAR) T-cell therapy, oncology nurses will need to be aware of the long-term effects of treatment that may persist into survivorship.

However, because the treatment is so new, studies measuring those patient-reported concerns are still forthcoming. The majority of today's recommendations for survivorship management are based on experts' clinical experience.

Two articles in the *Clinical Journal of Oncology Nursing*'s April 2019 supplement about CAR T-cell therapy addressed survivorship considerations in adult and pediatric patients and the nurse's role in managing them and developing survivorship care plans.

Late Effects of CAR T-Cell Therapy

Acute toxicities such as cytokine release syndrome and neurologic effects are typical concerns, but oncology nurses also need to watch for late effects and chronic toxicities, including cytopenias, infection, B-cell aplasia, and hypogammaglobulinemia.

Cytopenias: Before receiving CAR T cells, patients must undergo lymphodepleting chemotherapy, most commonly with cyclophosphamide and fludarabine, which are known to cause long-term cytopenia. Grade 3 or 4 anemia, thrombocytopenia, neutropenia, leukopenia, or lymphopenia can present up to 90 days postinfusion

and require transfusions or administration of growth-colony-stimulating factor.

Infection: Patients are at higher risk for infection with cytopenias. Studies have shown that 23%–42% of patients developed infections within the first 28-30 days after CAR T-cell treatment, 14% within 29–90 days, and 31% within 31–180 days. The infection risk persists until patients recover their B cells. Patients' blood counts should be monitored weekly for the first 60 days and as indicated thereafter until their blood counts recover. No recommendations currently exist regarding standardized antimicrobial prophylaxis.

Find podcasts, videos, articles, and other tools and resources for caring for patients receiving CAR T-cell therapy at ONS.org.

A related question is whether patients should be revaccinated following CAR T-cell therapy. Because vaccine immunity depends on B cells to form antibodies, patients with B-cell aplasia may not develop antibodies following CAR T-cell treatment. Although no current guidelines exist, Buitrago et al. advised revaccinating patients after B-cell recovery.

B-cell aplasia and hypogammaglobulinemia: Because patients' healthy B cells can be destroyed along with the malignant ones, CAR T-cell therapy may result in lineage depletion or B-cell aplasia and therefore chronic immunodeficiency.

Hypogammoglobulinemia occurred in 41% of patients 90 days after treatment in one study and may require immunoglobulin G (IgG) replacement, especially if patients develop frequent infections after therapy. IgG levels should be monitored monthly, and patients will need replacement for as long as CAR T cells persist.

Endocrine dysfunction: In younger patients especially, CAR T-cell therapy can affect the endocrine system. Patients who received prior treatment with allogenic stem cell transplantation or total body radiation are at higher risk for central and peripheral endocrine dysfunction, particularly related to the hypothalamus, thyroid, gonads, and adrenal glands, and Callahan et al. recommended that patients receive annual thyroid exams. For pediatric patients who are still growing, cranial radiation may first affect growth hormone levels.

Fertility: No studies have evaluated CAR T cells' effects on fertility or childbearing, Buitrago et al. said.

However, lymphodepleting chemotherapy may and patients of childbearing potential should consult with a fertility preservation specialist prior to initiating treatment. Most male and female patients will be infertile after total body radiation, Callahan et al. said. Males treated with cyclophosphamide may have germinal cell dysfunction but the majority will retain Leydig cell function.

Females will require ovarian function monitoring and a balance of estrogen replacement and growth hormone replacement.

Other Long-Term Effects of CAR T-Cell Therapy

Patients may have a potential to develop a secondary malignancy after CAR T-cell therapy and, according to U.S. Food and Drug Administration mandate, should be followed for 15 years after treatment. Pediatric patients are at risk for secondary malignancies even before starting CAR T-cell therapy because of prior treatments with etoposide, total body radiation, high-does cyclophosphamide, or cranial radiation. Liver, oral cavity, thyroid, cervical, skin, and breast cancer are the most common secondary cancers.

Callahan et al. recommended early mammography and breast magnetic resonance imaging in patients who received radiation to breast tissue.
Like many cancer treatments, CAR T-cell therapy is associated with fatigue: one trial reported that 51% of patients experienced the symptom, although it usually resolved within four to six weeks after infusion. ONS offers evidence-based recommendations for managing fatigue in patients with cancer at ons.org/pep/fatigue.

Seizures, weakness, confusion, aphasia, and coordination problems are some of the neurologic toxicities related to treatment, and as many as 5% of patients can experience neuropsychiatric disorders (e.g., depression, suicide attempts, myoclonic seizures, transient ischemic attacks). Patients should not drive for at least eight weeks post-infusion because of the risk of seizure-like activity. Prophylaxis with levetiracetam may be needed.

Because of its cost, CAR T-cell therapy may contribute to patients' financial toxicity. Although Medicare currently reimburses 50% and

that number could increase to 65% in 2020 under a new proposal, patients' ancillary expenses (e.g., transportation, travel accommodations, extra child care) can take a financial toll, Buitrago et al. said.

For more information on adult and pediatric survivorship considerations following CAR T-cell therapy and the opportunity to earn a total of 1.0 CNE contact hours, refer to the full articles by Buitrago et al. and Callahan et al.

Questions regarding the information presented in this article should be directed to the Clinical Journal of Oncology Nursing *editor at CJONEditor@ons.org*.