Journal of Blood Research & Hematologic Diseases

Commentary A SCITECHNOL JOURNAL

Immune-Related Adverse Events and Their Management in Patients with Acute Leukemia on Immunotherapy

Steinar Brekke*

Department of Health Sciences (DISSAL), University of Genova, Genova, Italy

***Corresponding author**: Steinar Brekke, Department of Health Sciences (DISSAL), University of Genova, Genova, Italy, E-mail: Johnson9@yahoo.com

Received date: 01 March, 2022, Manuscript No. JBRHD-22-59966;
Editor assigned date: 04 March, 2022, Pre QC No. JBRHD-22-59966 (PQ);
Reviewed date: 14 March, 2022, QC No. JBRHD-22-59966;
Revised date: 18 March, 2022, Manuscript No: JBRHD-22-59966 (R);
Published date: 28 March, 2022, DOI:10.4172/jbrhd.1000145.

Introduction

Acute leukemias, such as Acute Lymphoblastic Leukaemia (ALL) and Acute Myeloid Leukaemia (AML), are fast growing leukemias marked by high blast counts in the blood and bone marrow, as well as the primary malignant cell lineages. In the United States, an estimated 26,090 cases of acute leukaemia will be identified in 2020, with 12,700 deaths expected. Leukemia is the most frequent hematologic malignancy in children, and the prevalence of childhood leukaemia has been progressively rising each year. Over the last several decades, advances in molecular diagnostics have further defined multiple disease subtypes, which are distinguished by the presence of specific genetic markers, and have informed risk-based treatment paradigms to reduce toxicity in low-risk patients while pursuing more aggressive therapies for those at high risk of relapse. Standard acute leukaemia treatment paradigms have centred on high-intensity induction chemotherapy to achieve Complete Remission (CR), followed by allogeneic hematopoietic cell transplant (allo-HCT) to eradicate residual disease through the "graft versus leukaemia" effect mediated by the donor's immune cells in some patients. However, allo-HCT is not appropriate for all individuals, and a key ongoing difficulty in the area is that few chemotherapy-based treatments are viable after allo-HCT relapse or in patients with chemotherapy-resistant illness.

Immunotherapeutic techniques have transformed the therapy landscape for a wide range of diseases, including haematological malignancies. The US Food and Drug Administration (FDA) has recently approved novel agents such as monoclonal antibodies, bispecific antibodies, Antibody-Drug Conjugates (ADCs), and engineered (CAR) T cells, which provide additional options beyond standard regimens and deep and durable responses in some patients. Despite the fact that ADCs are not categorised as a typical form of immunotherapy, there is evidence that they have immunomodulatory properties. Despite the fact that immunotherapies for acute leukaemia have shown success in a number of large-scale, randomised trials, clinical experience with several of these innovative medicines remains limited. The Society for Immunotherapy of Cancer (SITC) published consensus recommendations on the use of immunotherapy in the treatment of haematological malignancies in December 2016 to support the oncology community and provide expert, evidence-based recommendations. Rapid breakthroughs in the area have since 2016, however, resulted in a greater range of immunotherapy-based treatment choices for each of the disease states described in the original guidelines: acute leukaemia, lymphoma, and multiple myeloma. As a result, the SITC Cancer Immunotherapy Guidelines—Hematologic Malignancies Subcommittee concluded that separate guidelines are required. SITC brought together a panel of experts to establish a new clinical practise guideline on the use of immunotherapy for the treatment of patients with acute leukaemia. This document is an update to a previously published consensus statement, based on a more recent analysis of peer-reviewed literature and clinical experience of expert panel members. These suggestions aren't meant to replace good clinical judgement; rather, they're meant to give doctors the most up-to-date information on how professionals integrate immunotherapy into the treatment of acute leukaemia patients.

Acute Leukemia Immunotherapy

Immune-related Adverse Events (AEs) are a major source of concern in immuno-oncology. Immunotherapies have distinct and serious side effects that must be managed with care. SITC has released a textbook on managing immunotherapy toxicity, as well as a consensus statement from the Toxicity Management Working Group on the management of toxicities after checkpoint inhibitor treatment. SITC published a review in 2018 on toxicity management after CAR T cell treatment for haematological malignancies. Two further SITC clinical practise guidelines for the recognition and management of immune-related adverse events for immune effector cell and checkpoint inhibitor medicines are in the works at the time of publication. The American Society for Transplant and Cellular Therapy has also released consensus guidelines for grading CRS and neurological damage following CAR T cell therapy.

AEs that occur during immunotherapy treatment for ALL are different and must be identified and addressed effectively as soon as possible. In the INO-VATE trial, 46 percent of patients treated with inotuzumab ozogamicin had grade 3 AEs, which was similar to the rate and profile of grade 3 AEs in individuals treated with SOC chemotherapy (43%). VOD occurred 11 percent (15 patients) more frequently in the inotuzumab ozogamicin group than in the standard-therapy group (1 patient). After the trial, 10 of the 48 patients in the inotuzumab ozogamicin group who underwent stem cell transplantation developed VOD. In the inotuzumab ozogamicin group, the median time to the onset of VOD after transplantation was 16 days (range, 3 to 39 days). Avoid HCT conditioning regimens containing dual alkylating agents, use prophylactic medicines in patients proceeding to HCT, limit treatment with inotuzumab ozogamicin to two cycles, monitor patient weight for fluid retention, and assess liver function frequently, according to recent consensus recommendations for the prevention and monitoring of VOD associated with inotuzumab ozogamicin. Both blinatumomab and CAR T cell treatments have the potential to cause major side effects, such as CRS and neurotoxicity. If not handled properly, these two events can be fatal. CRS was the most prevalent Adverse Event (AE) recorded across all CAR T cell clinical trials, with rates ranging from 74% to 100% for CD19-directed CAR T cells. CRS can manifest itself in a variety of ways. Fever, headache, rash, arthralgia, and myalgia are all mild signs of CRS. Hypotension can proceed to an uncontrolled systemic inflammatory response, necessitating vasopressors, circulatory shock, vascular leakage, disseminated intravascular coagulation, and multiorgan system failure in more severe situations. Supportive treatment and anti-IL-6 medicines to stop the cycle of

inflammation have been described in several descriptions of management methods for CAR T cell-associated CRS. CRS toxicity can be reduced by adjusting CAR T cell dose to reduce peak expansion and proliferation, as revealed in a recent study that used a fractionated dosing regimen to achieve high response rates and acceptable tolerability in adult patients with ALL. Nearly every study utilising CD19-directed T cells, including CAR T cells and blinatumomab, has found neurotoxicity. Neurotoxicity was reported in 25/267 (9.4%) of patients in the TOWER study testing blinatumomab for the treatment of ALL. In the ELIANA trial with tisagenlecleucel, 40 percent of patients (30/75) suffered a neurotoxic event of any grade, with 13 percent of patients (10/75) experiencing a grade 3 event. Extramedullary illness, young age, pre-existing neurological comorbidities, larger overall CAR T cell doses, early and/or severe CRS, and cytopenias are all risk factors for neurotoxicity after CAR T cell treatment. Neurotoxicity caused by CAR T cell treatment does not respond to tocilizumab, unlike CRS.