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Opinion Article

The Therapeutic Regimens for the Treatment of Acute Lymphoblastic Leukemia

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DESCRIPTION

Major developments in recent years have improved the prognosis for adults with Acute Lymphoblastic Leukemia (ALL). Our prognostic models have been improved as a result of the concept of measurable residual disease, which has also helped us make treatment decisions. Tyrosine kinase inhibitors that target BCR-ABL1, monoclonal antibodies that target CD20 (rituximab), antibody-drug conjugates that target CD22 (inotuzumab ozogamicin), bispecific antibodies (blinatumomab), and CD19 chimeric antigen receptor T cell therapy have revolutionised the treatment paradigms for ALL (tisagenlecleucel). These innovative methods that lessen dependency on rigorous cytotoxic chemotherapy and hematopoietic stem cell transplantation in the first remission are made possible by these new, very successful drugs. This in-depth analysis will concentrate on current developments and potential future prospects in innovative therapy approaches for adult ALL.

Various therapeutic regimens

The use of isotuzimab ozogamicin independently: The cytotoxic antibiotic calicheamicin is coupled to an anti-CD22 moAb called InO. InO was compared to conventional salvage chemotherapy in a phase 3 multicenter trial (INO-VATE) of 218 adult patients with CD22+ B cell ALL on the basis of encouraging phase I/II evidence. InO considerably outperformed chemotherapy in terms of total response and MRD negativity rates among responders (81% against 29%, P 0.001, and 78% versus 28%, P 0.001, respectively). Patients who received InO were more likely to be eligible for HSCT (41% as opposed to 11%; P 0.001). InO significantly increased both the median remission length and progression-free survival (4.6 against 3.1 months; P = 0.03; and 5.0 compared 1.8 months; P 0.001, respectively). The use of blinatumomab: A CD3/CD19 bispecific T cell engager moAb called blinatumomab has demonstrated high efficacy in R/R B cell ALL phase I/II investigations, especially when there is less disease burden. In adult patients with heavily pre-treated R/R B cell ALL, the phase 3 multicenter international study TOWER later demonstrated superiority of blinatumomab over standard salvage chemotherapy with higher CR rates (34% versus 16%; P 0.001), MRD negativity (76% versus 48%), and longer median OS (7.7 versus 4 months; P= 0.001). Regardless of age, the number of prior therapies, the preceding HSCT, or the percentage of bone marrow blasts, the effect was observed, however, it was more pronounced in first salvage (median OS 11.1 months versus 5.3 months).

Therapy using CAR (Chimeric Antigen Receptor) T cells: In R/R B cell ALL, CAR T cell treatment targeting CD19 has demonstrated excellent clinical effectiveness. Genetically altered autologous T cells produce antibodies against CD19+ leukemic cells. Based on the kind and quantity of co-stimulatory domains, there are now 4 generations of CARs, which enhance their proliferation and persistence *in vivo*. T cells are given into the patient after lymphodepletion chemotherapy in order to exert their direct cytotoxic effect and to harness both innate and adaptive immunity. 75 children and young adults with R/R CD19+ B cell ALL, 61% of whom had previously received HSCT, were included in a pivotal phase 2 multicenter research to assess the efficacy of a single infusion of tisagenlecleucel, a CD19 CAR T cell treatment.

CRS and neurotoxicity were the two adverse events of interest, occurring in 70% and 40% of cases, respectively. Although these side effects are frequently very serious, supportive medication, such as dexamethasone, tocilizumab (only for CRS), and anti-interleukin 6 antibodies, may usually manage them. Tisagenlecleucel has been approved for R/R CD19+ B cell ALL after two prior lines of therapy or in patients under the age of 25 who are unresponsive to first-line therapy as a result of this trial.

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