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Opinion Article

Role of Inotuzimab Ozogamicin and Blinatumomab Monotherapy in Acute Lymphoblastic Leukemia

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DESCRIPTION

Brivio, demonstrate in this issue of Blood that inotuzumab ozogamicin is safe and efficacious in pediatric patients with relapsed-refractory Acute Lymphoblastic Leukemia (ALL), with a phase 2 recommended doses of 1.8 mg/m^2. In the past ten years, significant progress has been achieved in the study of the disease pathophysiology and the creation of innovative ALL therapy. Major advances in the treatment of ALL have come from targeted treatments that target specific transcripts and leukemic cell surface antigens. Traditionally, R-R ALL is linked with terrible prognosis, with a cure rate of <10% in adult ALL and 30% in pediatric ALL. With a typical chemotherapy treatment, the Complete Remission (CR) rate for adult ALL is 30% to 40% for the first relapse and 20% to 25% for the second relapse. Brivio and colleagues present the findings of a phase 1 research of inotuzumab ozogamicin in pediatric R-R ALL. With an overall response rate of 80% and a 12-month survival rate of 40% in patients who had received a lot of prior treatment, this procedure was found to be both safe and effective (median number of courses given, 2; range, 1-4). Hepatic sinusoidal obstruction syndrome was present in two out of 23 patients (9%). The phase 2 dose was 1.8 mg/m^2, just like in adults. These outcomes matched those that the COG ALL0232 in 48 individuals reported. The 12-month survival rate was 40%, while the objective response rate was 62% 10.4% of patients who later underwent Allogeneic Stem Cell Transplantation (ASCT) experienced hepatic SOS (26% in those individuals).

Inotuzimab ozogamicin monotherapy

InO is an anti-CD22 moAb coupled to the cytotoxic antibiotic calicheamicin. 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 data. InO considerably outperformed chemotherapy in terms of total response and Measurable Residual Disease (MRD) negativity rates among responders (81% against 29%, P 0.001, and 78% versus 28%, P 0.001, respectively). Those 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). In comparison to 6.7 months, the median OS was 7.7 (P=0.04). Further follow-up on 326 patients showed 2-year OS rates of 23% against 10% (P=0.01) in favour of InO, which was later verified. The attainments of CR, MRD negative and consolidative HSCT were predictors for higher survival. Independent of the number of preceding therapies and they are obtained MRD negative experienced greater benefits. InO was related with higher hepatotoxicity including Veno-Occlusive Disease (VOD) but less hematologic and infectious problems compared with chemotherapy. Most frequently following HSCT and with the use of dual-alkylator conditioning, the VOD rate was 11% as opposed to 1% with chemotherapy.

Blinatumomab monotherapy

A CD3/CD19 bispecific T cell priority target to moAb called blinatumomab has demonstrated high efficacy in R/R B cell ALL phase I/II tests, especially in the presence of decreased disease load. 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). Neurotoxicity and Cytokine Release Syndrome (CRS), which were severe in 10% and 5% of cases, respectively, were the two adverse events of interest.

CONCLUSION

The positive outcomes with monoclonal antibodies, bispecific antibody complexes, and CAR T cells offer crucial therapeutic tools to enhance outcomes for ALL patients. These therapeutic

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approaches are complimentary rather than competitive. To achieve the deepest and highest levels of remission, they might be given one after the other. Their continuous rational combination in the frontline situation may help many patients avoid long-term intense chemotherapy and Autologous Stem Cell Transplant (ASCT). Rarely is a Splenectomy necessary for acute lymphoblastic leukemia. Splenectomy can increase platelet count but has no impact on how leukemia will manifest itself. Splenectomy can be used to address severe symptoms such stomach pain that are resistant to chemotherapy. In most instances, radiation can also be utilized to try and shrink the size of an enlarged spleen.