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Commentary

# Blinatumomab may be Feasible at All Stages of B-Cell Acute Lymphoblastic Leukemia

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## ABOUT THE STUDY

B-Cell Acute Lymphoblastic Leukemia (B-ALL) is a common malignant hematological neoplasm in which B-lineage lymphocytes are blocked at an early stage of differentiation and development resulting in abnormal clones of immature cells that can involve bone marrow, peripheral blood and other extramedullary sites. In recent years, the outcome of B-ALL has been significantly improved due to advancements in various treatment methods which include the use of child-like chemotherapy regimens in adults, small molecule targeted drugs, and the advancement of Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT). However, many adults (about 50%-65%) and a small proportion of pediatric patients (about 10%-20%) develop chemotherapy resistance or relapse during treatment, and the re induction rate of Complete Remission (CR) by conventional chemotherapy is only 20%-30% [1-2]. Fortunately, novel immunotherapy methods provide great potential for the treatment of B-ALL, showing highly promising response and cure rates. Although immunotherapy may have associated toxicities, these are generally manageable and the Treatment-Related Mortality (TRM) rate is low, estimated at around 1% [3]. Various immunotherapeutic strategies have been applied to B-ALL, initially focusing on relapsed or refractory (r/r) ALL and patients with Minimal Residual Disease (MRD), and gradually emerging in different disease settings of B-ALL.

Blinatumomab, a bispecific antibody that binds both CD19 and CD3, can link CD19+ B cells to CD3+ T cells and redirect T cell-mediated cytotoxicity to CD19+ B cells leading to B-cell lysis. CD19 is widely expressed in B-cell lineage cancer cells, so it is an ideal target for B-ALL. We have evaluated the efficacy and safety of blinatumomab monotherapy for the treatment of r/r B-ALL. A total of 18 studies involving 1,373 patients were included. The analysis results showed a CR rate of 54% (95% CI: 44%-64%) and an MRD response rate of 43% (95% CI: 34%-51%) [4]. Also, blinatumomab is applicable to B-ALL in other disease states. A single-center phase 2 study evaluated the feasibility of 4 cycles of blinatumomab administered every 3 months during the first year after allogeneic Hematopoietic Cell Transplantation (HCT) among to reduce recurrence in high-risk ALL patients. With a median follow-up of 14.3 months, the 1-year Overall Survival (OS), Progression-Free Survival (PFS), and Non-Relapse Mortality (NRM) rates were 85%, 71%, and 0%, respectively. It was found that blinatumomab postallogeneic HCT is feasible [5]. A phase III trial was conducted to randomize newly diagnosed Ph-B-ALL patients (aged 30-70 years) into two groups: Receiving conventional chemotherapy alone or along with blinatumomab. The objective was to determine whether patients who achieved Minimal Residual Disease (MRD) negativity (<0.01%) after induction chemotherapy would experience enhanced outcomes with the addition of blinatumomab. 224 MRD negtive patients were randomized (112 in each group). Blinatumomab group received four additional cycles of blinatumomab during consolidation therapy. The control group received four cycles of consolidation chemotherapy alone. Median Overall Survival (OS) of blinatumomab arm was not reached *versus* 71.4 months of the control arm. Median follow-up was 43 months. The addition of belintuzumab to consolidation chemotherapy is expected to become a new standard of treatment for newly diagnosed older patients with Ph-B-ALL [6].

## CONCLUSION

Immunotherapy is a great challenge in the treatment of B-ALL, and current research mainly focuses on CD19 and CD22. Fortunately, for the major antigens expressed, antibody therapies are available. In addition to these two targeted drugs, we also need to consider whether there are backup therapeutic drugs. In the future, if we can develop more targets aiming at specific genes or proteins of different ALL subtype, and then design specific inhibitors or agonists to inhibit the proliferation and survival of leukemia cells, or induce tumor cell differentiation and apoptosis; we will get improved treatment outcomes.

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