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TARGETED THERAPIES

New standard for relapsed ALL

The overall survival duration of patients with relapsed or refractory acute lymphoblastic leukaemia (ALL) is <6 months; a major treatment goal in this heavily-pretreated population is to induce remission to enable patients to undergo stem-cell transplantation. The surface antigen CD19 is expressed on >90% of ALL cells, making this an attractive therapeutic target. The bispecific T-cell engager antibody blinatumomab binds to CD19-positive ALL cells, enabling the patient's own endogenous T cells to recognize and eliminate ALL blast cells. In a phase II study, this agent showed encouraging efficacy in patients with ALL. Now, the results of a phase III randomized trial demonstrate that blinatumomab significantly improves overall survival compared with that observed with standard-of-care chemotherapy.

In total, 405 patients with heavily pretreated ALL were randomly assigned in a 2:1 ratio to receive blinatumomab or chemotherapy. Overall survival was significantly longer (7.7 months versus 4 months) in the blinatumomab arm. The complete remission rate 12 weeks after therapy initiation (34% versus 16%), and the event-free survival (31% versus 12%) were also significantly higher in patients receiving blinatumomab compared with chemotherapy. Importantly, the duration of remission was prolonged (7.3 months versus 4.6 months) with blinatumomab. Adverse events of grade 3 or higher were lower in the blinatumomab group (87% versus 92%).

Hagop Kantarjian, lead author of the study, comments on these findings: "these randomized trial data enhance the notion that monoclonal antibody therapies will play a significant part in improving outcomes in ALL". These promising results have implications for future research: "We should investigate blinatumomab and other monoclonal therapies in combination with chemotherapy as both salvage and frontline treatments in adults with ALL," concludes Kantarjian.

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ORIGINAL ARTICLE Kantarjian, H. M. *et al.* Blinatumomab versus chemotherapy for advanced acute lymphoma leukemia. *N. Engl. J. Med.* **376**, 836–847 (2017)