Blinatumomab Shows Superiority Over Chemotherapy in Advanced Acute Lymphoblastic Leukemia

Blinatumomab, an anti-CD19 bispecific T-cell engager had a significant survival advantage compared with chemotherapy, in a randomized, open-label phase III trial.

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January 22, 2018 – In patients with Philadelphia chromosome (Ph)-negative B-cell precursor acute lymphoblastic leukemia (ALL), blinatumomab extended overall survival and hematologic remission compared with chemotherapy, according to the findings of a phase III trial.

Hagop Kantarjian, MD, with the Department of Leukemia, University of Texas M.D. Anderson Cancer Center, Houston, and colleagues reported their findings in the Mar 2, 2017, issue of the *New England Journal of Medicine*.

Blinatumomab binds to CD3-positive cytotoxic T cells and CD19-positive B cells at the same time. This process enables the patient's T cells to identify and destroy CD19-positive ALL blasts.

Previous single-group phase 2 studies demonstrated the efficacy and safety of blinatumomab. In one such pivotal multicenter study, the rate of complete remission with complete or partial hematologic recovery was 43%, with 6.1 months median overall survival.

The current multinational phase 3 study was designed to compare blinatumomab with standard chemotherapy for the treatment of patients with recurrent or resistant ALL. A total of 405 patients 18 years or older, with ALL were randomized 2:1 to receive either blinatumomab or chemotherapy.

The primary end point was overall survival. The key secondary end points included event-free survival and achievement of complete remission either with full hematologic recovery or with full, partial, or incomplete hematologic recovery within 12 weeks after initiation of treatment.

Blinatumomab resulted in longer median overall survival relative to chemotherapy (7.7 vs 4.0 months; hazard ratio [HR] 0.71, 95% CI 0.55 to 0.93; P = 0.01).

Remission rates within 12 weeks after initiation of treatment were significantly higher in the blinatumomab arm relative to the chemotherapy arm, both in patients with full hematologic recovery (34% vs 16%, P < 0.001) and patients with full, partial, or incomplete hematologic recovery (44% vs 25%, P < 0.001).

Compared with those on chemotherapy, patients who received blinatumomab had a higher rate of event-free survival (6-month estimates, 31% vs 12%; HR, 0.55, 95% CI, 0.43-0.71; P < 0.001) and longer median duration of remission (7.3 vs 4.6 months). A total of 24% of the patients in each treatment arm had allogeneic stem-cell transplantation.

Adverse events of grade 3 or higher were more common in patients in the chemotherapy group compared with blinatumomab group (92% vs. 87%).

“In this trial, the use of two central laboratories with different methods for assessing minimal residual disease may have introduced a variable that could limit interpretation of the trial,” the authors noted.

The investigators concluded that “the activity of an immune-based therapy such as blinatumomab, which depends on functioning T cells for its activity, provides encouragement that responses may be further enhanced and made durable with additional immune activation strategies.”

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