Durability of CAR T-cell therapy response may depend on pretreatment disease burden in leukemia patients

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Although most patients with relapsed B-cell acute lymphoblastic leukemia (B-ALL) experienced complete response after treatment with a type of CAR T-cell immunotherapy, pretreatment disease burden impacted the durability of the responses and long-term survival, according to data from a clinical trial presented here at the AACR Annual Meeting 2017, April 1-5.

"Adult patients with relapsed or refractory ALL have extremely poor outcomes, with the five-year survival rate being less than 10 percent. Therefore, there is a clear need to develop effective therapy for these patients," said Jae Park, MD, assistant attending physician at Memorial Sloan Kettering Cancer Center (MSKCC) in New York.

"To this end, we and other groups have developed and tested CD19-specific CAR T-cell therapy [19-28z CAR T-cell therapy] and have reported encouraging results, with high initial complete response rates in patients with B-ALL. However, relapses are common, even after achieving seemingly deep remission, and severe toxicities have been observed in some patients," Park noted.

Park and colleagues, therefore, retrospectively analyzed data from a prospective clinical trial that tested 19-28z CAR T-cell therapy to identify patients who benefited the most from this therapy. All of the 51 adult patients in this trial had relapsed or refractory B-ALL after one or

more conventional multiagent chemotherapy.

The researchers measured disease burden prior to CAR T-cell infusion in all patients and divided them into two cohorts – those who had minimal residual disease (MRD) with less than 5 percent blast cells in bone marrow (20 patients), and those who had morphologic disease, with 5 percent or more blast cells in bone marrow (31 patients).

Complete response rates in the MRD cohort and morphologic disease cohort were 95 percent and 77 percent, respectively, which was not statistically different. After a median of 18 months of follow-up, median event-free survival and overall survival could not be computed for those in the MRD cohort (because most patients were still disease-free and alive), but they were 6.3 months and 17 months, respectively, for those in the morphologic disease cohort.

The study also found that long-term survival did not improve for patients in either cohort by having a hematopoietic stem cell transplant (HSCT) after CAR T-cell therapy.

"While more patients and longer follow-up will be needed to adequately address the significance of HSTC, the result of this analysis raises a question as to whether 19-28z CAR therapy can be considered as a definitive, curative therapy rather than a bridge to stem cell transplant, at least in a subset of patients," Park noted.

"Our data suggest that incorporation of 19-28z CAR T cells at the time of MRD following first-line chemotherapy will maximize the durability of CAR T-cell mediated remissions and survival and can potentially spare these high-risk patients from HSCT, rather than waiting until they relapse morphologically and then trying CAR T-cell therapy when it is less likely to achieve a durable long-term outcome," Park added.

Patients from the MRD cohort fared well in terms of side effects as well, compared with those in the morphologic disease cohort. Two of the major side effects associated with CAR T cells, cytokine release syndrome (CRS) and neurotoxicity, occurred in 42 percent and 58 percent of the patients, respectively, in the morphologic disease cohort, compared with 5 percent and 15 percent, respectively, in those from the MRD cohort. No case of cerebral edema was observed in either cohort of this study, Park noted.

A limitation of the study is that this is a retrospective analysis and the findings will need to be validated prospectively, Park said. Further, the analysis on the impact of post-CAR allogeneic HSCT was limited by a relatively small sample size in each cohort as the study was not designed to specifically answer or address that question.

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