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New type of targeted therapy shows promise in preclinical models of B-cell malignancy

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An investigational, bacterial toxin-based therapy targeted to the protein CD38, which is found on the surface of many human blood cancer cells, including multiple myeloma cells, dramatically increased survival in mice bearing human tumor cells, according to data presented at the American Association for Cancer Research special conference, Hematologic Malignancies: Translating Discoveries to Novel Therapies, held Sept. 20-23.

"Although there are treatment options for patients with multiple myeloma, there is currently no cure, and many patients receive multiple treatments to manage the disease," said Erin K. Willert, PhD, executive vice president of research and development at Molecular Templates Inc. in Georgetown, Texas. "In this study, we found that the growth of human cancer cells in mice was substantially decreased, or the cells were even eliminated, following treatment with our investigational CD38-targeted therapy.

"Our results give us confidence in moving the drug forward toward clinical trials for CD38-positive B-cell malignancies such as multiple myeloma," continued Willert. "Moreover, since our CD38-targeted engineered toxin body works differently than current therapeutics, we think that our investigational therapy has the opportunity to be effective in cases of relapsed or refractory multiple myeloma and other CD38-positive B-cell malignancies."

The investigational therapy studied by Willert and colleagues is a

CD38-targeted engineered toxin body. According to Willert, engineered toxin bodies recognize a specific protein on the surface of a cancer cell, CD38 in the case of this investigational therapy, and deliver a modified bacterial toxin that enters the cancer cell and then shuts down protein production and kills the cell.

In mice bearing human cancer cells, the lowest dose of the investigational CD38-targeted engineered toxin body (0.05 mg/kg body weight) significantly reduced tumor burden: Mean tumor burden was 29 percent of the burden in control mice. Treatment with higher doses, 0.5 and 2 mg/kg, resulted in mean tumor burden of less than 1 percent of control.

The investigational CD38-targeted engineered toxin body increased median survival. Control mice had a median survival of 34 days compared with 59.5 days for mice treated with the lowest dose of the investigational therapy. Among mice who received 0.5 or 2 mg/kg of the investigational therapy, 90 percent and 100 percent were alive at day 60 of the study, respectively.

"Based on comparisons with another engineered toxin body therapy that is entering clinical testing, we believe the concentrations of the investigational CD38-targeted engineered toxin body we used in the mice in this study will be relevant to the doses used in humans," said Willert. "However, more preclinical studies are needed before we can test the therapy in the clinic."

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