多発性骨髄腫に対する新たなタイプの免疫療法 (Abstract LBA3001)

CAR T細胞療法は多発性骨髄腫を長期寛解に持ち込む

CAR T-cell therapy sends multiple myeloma into lasting remission

2017年American Society of Clinical Oncology年次集会で発表された早期臨床試験において、多発性骨髄腫患者35人中33人（94%）が新たなタイプの免疫療法－B細胞成熟蛋白BCMAを標的としたキメラ抗原受容体（CAR）T細胞－を受けることにより臨床的寛解を得た。治療効果を示す最初の徴候はCAR T細胞の初回注射から10日と、早期に出現した。CAR-T細胞療法は、各患者に対し個別に作成される。患者自身のT細胞が収集され、ラボで遺伝子の再構成が行われ、患者に注射し戻される。多くの患者は、軽度の副作用を発現するのみである。

Full Text

In an early clinical trial, 33 out of 35 (94%) patients had clinical remission of multiple myeloma upon receiving a new type of immunotherapy - chimeric antigen receptor (CAR) T cells targeting B-cell maturation protein or BCMA. Most patients had only mild side effects.

The study was presented in at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Although recent advances in chemotherapy have prolonged life expectancy in multiple myeloma, this cancer remains incurable," said study author Wanhong Zhao, MD, PhD, an associate director of hematology at The Second Affiliated Hospital of Xi'an Jiatong University in Xi'an, China. "It appears that with this novel immunotherapy there may be a chance for cure in multiple myeloma, but we will need to follow patients much longer to confirm that."

CAR T-cell therapy is custom-made for each patient. The patient's own T cells are collected, genetically reprogrammed in a lab, and injected back into the patient. The reprogramming involves inserting an artificially designed gene into the T-cell genome, which helps the genetically reprogrammed cells find and destroy cancer cells throughout the body.

Over the past few years, CAR T-cell therapy targeting a B-cell biomarker called CD19 proved very effective in initial trials for acute lymphoblastic leukemia (ALL) and some types of lymphoma, but until now, there has been little success with CAR T-cell therapies targeting other biomarkers in other types of cancer. This is one of the first clinical trials of CAR T cells targeting BCMA, which was discovered to play a role in progression of multiple myeloma in 2004.

The authors report results from the first 35 patients with relapsed or refractory multiple myeloma enrolled in this ongoing phase I clinical trial in China. First signs of treatment efficacy appeared as early as 10 days after initial injection of CAR T cells (patients received three split doses of cells over a week). Overall, the objective response rate was 100% and 33 (94%) patients had an evident clinical remission of myeloma (complete response or very good partial response) within two months of receiving CAR T cells.

To date, 19 patients have been followed for more than four months, a pre-set time for full efficacy assessment by the International Myeloma Working Group (IMWG) consensus. Of the 19 patients, 14 have reached stringent complete response (sCR) criteria, one patient has reached partial response, and four patients have achieved very good partial remission (VgPR) criteria in efficacy.

There has been only a single case of disease progression from VgPR; an extramedullary lesion of the VgPR patient reappeared three months after disappearing on CT scans. There has not been a single case of relapse among patients who reached sCR criteria. The five patients who have been followed for over a year (12-14 months) all remain in sCR status and are free of minimal residual disease as well.

Cytokine release syndrome or CRS, a common and potentially dangerous side effect of CAR T-cell therapy, occurred in 85% of patients, but it was only transient. In the majority of patients symptoms were mild and manageable. CRS is associated with symptoms such as fever, low blood pressure, difficulty breathing, and problems with multiple organs. Only two patients on this study experienced severe CRS (grade 3) but recovered upon receiving tocilizumab (an inflammation-reducing treatment commonly used to manage CRS in clinical trials of CAR T-cell therapy). No patients experienced neurologic side effects, another common and serious complication from CAR T-cell therapy.

"While it's still early, these data are a strong sign that CAR T-cell therapy can send multiple myeloma into remission," said ASCO Expert Michael S. Sabel, MD, FACS. "It's rare to see such high response rates, especially for a hard-to-treat cancer. This serves as proof that immunotherapy and precision medicine research pays off. We hope that future research builds on this success in multiple myeloma and other cancers."

The researchers plan to enroll a total of 100 patients in this clinical trial, at four participating hospitals in China. "In early 2018 we also plan to launch a similar clinical trial in the United States. Looking ahead, we would also like to explore whether BCMA CAR T-cell therapy benefits patients who are newly diagnosed with multiple myeloma," said Dr. Zhao.

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