子宮頸がんにおけるT細胞免疫療法（Abstract: LBA3008）

HPV標的養子T細胞療法は進行子宮頸がんに対する個別化医療となる可能性がある

HPV-targeted adoptive T-cell therapy may provide a personalized strategy for advanced cervical cancer

第50回American Society of Clinical Oncology学会で発表された第II相研究から、進行子宮頸がんに対し養子T細胞療法として知られる新たな個別化免疫療法を施行された複数の女性において、注目すべき結果が得られたことが示された。HPV標的養子T細胞療法は、腫瘍内のHPVに対する自然免疫応答を本質的に増幅させる。今回のスタディにおいて、9人の患者が養子T細胞療法を受け、うち3人が治療に奏効を示した。1人の患者は部分寛解し、腫瘍体積が39%減少し、2人の患者は完全寛解した。これら2人の患者は広範な転移を有しており、以前の治療にもかかわらず子宮頸がんが増悪していた。解析の時点で、これら2人の患者は治療後11か月および18か月寛解状態が持続していた。この治療には重篤な副作用があり、最も多かったのが血球数減少、感染症、および代謝障害であった。養子T細胞療法が子宮頸がんに対し検証されたのは今回が初めてである；過去にはメラノーマ、白血病、およびサルコーマにおいて有望であることはすでに示されている。研究者らは今回のスタディを拡大しさらに患者を組み入れることを計画している。このスタディではまた、咽喉がんや肛門がんなど他のHPV関連がんの治療としての養子T細胞療法に関しても調査している。

Full Text

A small phase II study shows striking results in several women with advanced cervical cancer, using a new type of personalized immunotherapy, known as adoptive T-cell therapy. In the study, two patients with widespread metastases had complete remissions after a single treatment with the HPV-targeted T-cells, and have been cancer free for nearly a year or longer.

"This proof-of-principal study shows that adoptive transfer of HPV-targeted T-cells can cause complete remission of metastatic cervical cancer and that this remission can be long-lasting," said lead study author Christian Hinrichs, M.D., an assistant clinical investigator at the National Cancer Institute in Bethesda, M.D.. "One implication of the study is that cellular therapy might have application to a broader range of tumor types than previously recognized. This treatment is still considered experimental and is associated with significant side effects. We also need to explore why this therapy worked so well in certain women, and not in others."

Women with metastatic cervical cancer – caused by the human papillomavirus (HPV) – have limited treatment options. The median survival with the two standard first-line therapies, chemotherapy and a combination of chemotherapy and bevacizumab, is 13 and 17 months, respectively. No second-line treatments that improve survival are available.

HPV-targeted adoptive T-cell therapy essentially augments the natural immune response to HPV in the tumor. To develop the therapy, HPV-targeted T-cells are grown from a patient's tumor in the laboratory. Those cells are subsequently infused back into the patient to fight the cancer. This is the first time adoptive T-cell therapy has been tested in cervical cancer; it has previously shown promise in melanoma, leukemia, and sarcoma.

In the study, nine patients received adoptive T-cell therapy, and three responded to the treatment. One patient had a partial response, with a 39-percent reduction in tumor volume, and two patients had complete remissions. Those two patients had widespread metastases, and the disease had progressed despite prior therapy. At the time of analysis, those patients remained in remission for 11 and 18 months after treatment. The treatment was associated with serious side effects, the most common being low blood counts, infections, and metabolic disorders.

Researchers are planning to expand this study to enroll additional patients. The same study is also exploring adoptive T-cell therapy for treatment of other HPV-related cancers, such as throat cancer and anal cancer.

Adoptive T-cell therapy is being offered at an increasing number of major medical centers in the United States and other countries. Along with screening and preventative vaccines, better treatments are needed to reduce cervical cancer deaths in the future.

"Novel treatments are needed for women with recurrent or metastatic cervical cancer. Because of the association between cervical cancer and the HPV virus, adoptive immunotherapy is a promising approach for these patients," said Don S. Dizon, M.D., FACP, ASCO Expert. "These preliminary data demonstrate, not only the viability of this approach, but that gains in survival can be realized in a cancer where patients have little to no effective treatment options and where median survival is usually less than two years."

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