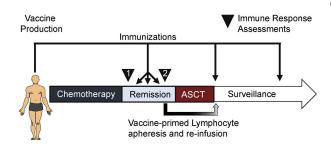


Early clinical trial supports tumor cell-based vaccine for mantle cell lymphoma

19 June 2020



A schematic of the vaccination schedule used to treat MCL patients in the phase I/II trial. ASCT stands for autologous stem cell transplantation. Credit: Frank et al., 2020

A phase I/II clinical trial by researchers at Stanford University suggests that vaccines prepared from a patient's own tumor cells may prevent the incurable blood cancer mantle cell lymphoma (MCL) from returning after treatment. The study, which will be published June 19 in the *Journal of Experimental Medicine* (*JEM*), reveals that the vaccines are a safe and effective way to induce the body's immune system to attack any tumor cells that could cause disease relapse.

MCL is an aggressive form of non-Hodgkin lymphoma in which white blood cells known as B cells become cancerous and form tumors in the lymph nodes and other parts of the body. The disease is generally treated with a combination of chemotherapy and immunotherapy, often accompanied by a hematopoietic stem cell transplant to restore the body's ability to form normal, healthy blood cells. But the cancer usually returns, and the average survival time for MCL patients is 5-7 years.

Ronald Levy and colleagues at Stanford University previously developed a tumor cell-based vaccine that prevents lymphomas from recurring in mice. Tumor cells isolated from the mice are loaded with

CpG oligonucleotides, short fragments of DNA that mimic bacterial DNA and can prompt an immune response against the cells when they are injected back into the mice. "Guided by these preclinical results, we designed a phase I/II clinical trial (NCT00490529) to evaluate the therapeutic potential of a similar vaccination approach as an additive to standard stem cell transplantation for patients with MCL," Levy says.

In the trial, 47 MCL patients who had achieved remission through standard immune- and chemotherapies were vaccinated with their own, CpG-loaded, tumor cells. The patients' immune cells were then collected and saved while the patients received a stem cell transplant. Finally, the immune cells were transferred back into the patients, who were then monitored for signs of their MCL returning.

The vaccination regimen appeared to be safe, causing no side effects beyond those normally associated with stem cell transplants. Over the following year, 89% of the patients remained free of minimal residual disease (MRD), meaning that their blood contained too few cancer cells to form any new tumors. "That surpasses previously reported MRD-free rates for MCL patients," Levy says.

Of the patients, 40% formed immune cells capable of directly attacking and killing cancer cells. These patients appeared to be especially well protected from disease relapse, going much longer without any recurrence of MCL, even if their tumors contained genetic mutations associated with a poor prognosis.

"Overall, our data demonstrate that the addition of a CpG-activated whole cell tumor vaccination followed by adoptive transfer of vaccine-primed immune cells to the treatment of MCL is feasible, safe, and can induce immune responses that are associated with a superior clinical outcome," Levy says. The researchers are now considering ways to



improve the <u>immune response</u> to tumor cell vaccination still further.

More information: Frank et al., 2020. *J. Exp. Med.* rupress.org/jem/article-lookup ... 10.1084/jem.20191712

Provided by Rockefeller University Press

APA citation: Early clinical trial supports tumor cell-based vaccine for mantle cell lymphoma (2020, June 19) retrieved 17 July 2022 from https://medicalxpress.com/news/2020-06-early-clinical-trial-tumor-cell-based.html

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