Nature Reviews Drug Discovery | Published online 30 May 2018; doi:10.1038/nrd.2018.85

Steve Allen Travel Photography/Alamy Stock Photo

CANCER

Personalized cancer vaccines hit the spot

The potential to generate antitumour immune responses using tumour lysates has been an attractive proposition for many years, but previous efforts have not been successful. Now, Tanyi et al. describe a vaccine — generated with autologous dendritic cells (DCs) pulsed with tumour lysate — that elicits antitumour responses and prolongs survival in patients with recurrent ovarian cancer.

Ovarian cancers express a multitude of tumour-specific antigens and are therefore immunoreactive. Despite the expression of tumour-specific antigens, results from immunotherapy, specifically antibodies to programmed cell death protein 1 (PD1) or PD1 ligand 1 (PDL1), have been modest in patients with ovarian cancer. Indeed, T cells are unable to home in on ovarian tumours, possibly because of a vascular–endothelial barrier that forms in response to vascular endothelial growth factor A (VEGFA).

> “the 2-year overall survival rate was 100%”

As an alternative approach, Tanyi et al. previously developed autologous DCs pulsed with autologous whole-tumour lysate from single cells that had been killed with hypochlorous acid and lysed using freeze–thaw cycles; this treatment was efficacious in preclinical models. In their new work, they combine this DC vaccine with the intravenous VEGFA-blocking antibody, bevacizumab (to allow the activated T cells to enter the tumour) and low-dose cyclophosphamide (to dampen the response of regulatory T cells) in a clinical trial.

DC vaccines were prepared from 25 platinum-pretreated, immunotherapy-naive patients with recurrent advanced epithelial ovarian cancer, and administered through a direct bilateral intranodal injection. In total, 5 patients received the vaccine alone, 10 patients received the vaccine plus bevacizumab and 10 patients received the vaccine, bevacizumab and cyclophosphamide.

The clinical response correlated most strongly with whether the patient mounted an immune response to the vaccine and with the use of cyclophosphamide. In 11 out of 22 evaluable patients, T cells that produced interferon-γ (IFNγ) and responded to DC-presented tumour antigens could be detected in peripheral blood mononuclear cells (PBMCs) collected 5 days after vaccination. Many of these cells responded to tumour-specific neoepitopes, and the presence of neoepitope-specific T cells increased after vaccination. These responses were largely specific to the mutated protein and not the wild-type counterpart. Some of these cells were novel, dominant T cell clones with high avidity T cell receptors.

Patients with tumour antigen-reactive T cells had significantly longer progression-free survival than did those without; 8 of the 11 patients who mounted an immune response to tumour antigens had a longer complete response on this therapy than on their previous treatment (remission inversion) and the 2-year overall survival rate was 100% (compared with 25% in the non-responders).

Cyclophosphamide also increased the fraction of patients that generated an immune response (8 out of 10 versus 3 out of 12). The 2-year overall survival of patients treated with all three drugs was 80%; a historic control group that received bevacizumab and cyclophosphamide had a 2-year survival of 44%.

These data suggest that DC vaccines generated from autologous tumour cell lysates could be useful in the treatment of certain immunoreactive tumours, particularly in combinatorial approaches.

Megan Cully

ORIGINAL ARTICLE Tanyi, J. L. et al. Personalized cancer vaccine effectively mobilizes antitumor T cell immunity in ovarian cancer. *Sci. Transl Med.* **10**, eaao5931 (2018)