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"A Phase 1b Safety and Feasibility Study of Personalized Immunotherapy in Adults with Advanced Cancers"

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SCIENTIFIC ABSTRACT

Recognition of non-self antigens is the basis of vigorous anti-tumor immune responses. In fact, multiple lines of evidence confirm that the efficacy of immune checkpoint blockade is based on the ability to reinvigorate a T cell response against cancer neoantigens. We have developed, through a collaboration between MCC and LJI, a novel neoantigen discovery pipeline that enables rapid identification and functional validation of immunogenic neo-epitopes, irrespective of tumor mutational burden, that does not rely on conventional in silico prediction models. We have now harnessed this methodology to develop personalized neoantigen synthetic long peptide vaccines. We propose to conduct an investigator initiated phase 1b clinical trial to test the feasibility and tolerability of the vaccine in combination with the anti-PD1 antibody pembrolizumab in patients with metastatic cancer. In addition, immunologic monitoring during the study will allow us to assess neoantigen specific T cell responses to the vaccine as well as the ability of the vaccine and pembrolizumab to induce de-novo priming of T cells against additional neoantigen targets, i.e. "epitope spreading." This clinical trial will validate the neoantigen discovery pipeline developed at UCSD and LJI, lay the foundation for personalized immunotherapy, and provide critical preliminary data to perform additional clinical trials testing the efficacy of this approach in patients with metastatic disease and at preventing cancer recurrence following definitive therapy.

LAY ABSTRACT

Immunotherapy has produced a paradigm shift in the way we approach and manage cancer. In the last few years we have seen unprecedented improvements in cancer survival stemming from immunotherapy with corresponding expedited drug approvals by the FDA. These agents are generally well tolerated and can have deep and enduring responses once immune recognition of the tumor has occurred. Unfortunately, over 80% of cancer patients do not benefit from current immunotherapies because the available drugs are ineffective at inducing immune rejection of the tumor. Accordingly, we hypothesized that if a patient's immune system is stimulated to recognize their cancer then a vigorous anti-tumor response can be achieved. Over the last four years, we have developed a method of identifying targets in a patient's cancer that can be seen by their immune system, so called "neoantigens". We are now taking this discovery to the clinic by conducting a clinical trial using a personalized neoantigen vaccine in combination with standard immunotherapy. The clinical trial will test the feasibility of creating truly individualized cancer vaccines and demonstrating the efficacy of this approach at inducing immune responses against a patient's cancer. This study will lay the groundwork for larger trials for patients with metastatic cancer, irrespective of the primary tumor site, and for studies testing the effectiveness of personalized cancer vaccines at preventing cancer recurrence after definitive therapy. This work will usher in a new era of transformational immunotherapy that is precise, tailored to the patient, and with little to no side effects.