BREAKTHROUGH PROGRAM

Sehha

SEHHA

Founder
Ahmed Al-Qahtani Ph.D.
KFSH&RC

Co-Founder
Reid Rubsamen MD, MS, MHCM
CEO, Flow Pharma

Team Member
Anthony Tufaro MD
Cleveland Clinic

Startup Brief

Unfortunately, up to 70 percent of all organ transplant recipients will be affected squamous-cell or basal cell type skin carcinomas and the incidence of these carcinomas increases with the duration of immunosuppressive therapy, The etiology of these neoplasms has been traced to infection with human papilloma virus (HPV) types 8 , 5, 16 and 15. These HPVs are detectable in 30% of skin squamous cell carcinomas (SCC) from immunocompetent individuals, rising to 90% in transplant recipients with SCCs. Currently available HPV vaccines do not target all of the HPV strains responsible for skin cancer and were not designed to treat patients already infected with HPV. Flow Pharma has developed a microparticle T cell vaccine targeting the HPV E7 protein believed to drive malignant transformation in transplant associated skin cancers. The central hypothesis of this proposal is that targeting HPV type 5, 8,15 and 16 E7 protein, HPV + (e.g., by PCR) cells (both preneoplastic and transformed) for cytotoxic CD8+ T cell attack following vaccination with the FlowVax-HPV cancer immunotherapy vaccine will provide meaningful protection against skin cancer associated with immunosuppression and transplantation. This proposal will take the immunotherapy through IND filing in the US and the Kingdom of Saudi Arabia.

Problem

The current cohort of transplant recipients under immunosuppression have not received a prophylactic HPV vaccine prior to 2006 (date of the first HPV vaccine FDA approval). The global pooled HPV prevalence is about 31% for any HPV and 21% for high-risk HPV. HPV-16 was the most prevalent HPV genotype (5%) followed by HPV-6 (4%). Current HPV vaccines (i.e., Gardasil and Cervarix) are prophylactic antibody inducing vaccines targeting the L1 capsid protein and do not induce effective T cells responses against latently infected SCC tumor cells.

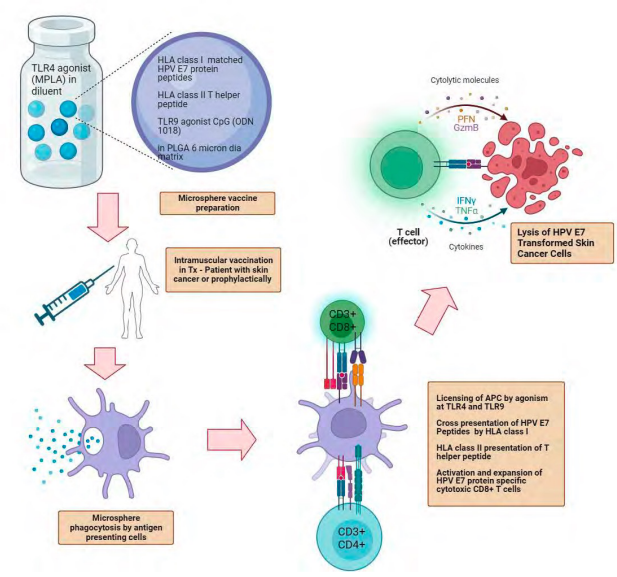

Figure 1. FlowVax adjuvanted microspheres containing HLA class I and HLA class II peptide antigens from the tumor associated protein survivin are suspended in diluent containing a second adjuvanted are injected into a cancer patient. The microspheres are taken up by antigen presenting cells, and through cross presentation, T-cell expansion occurs. These cytotoxic T-cells circulate and bind to survivin peptide antigens displayed on the cancer cell surface, subsequently destroying the cancer cell.

Solution

The unique proposition of the FlowVax-HPV cancer vaccine immunotherapy for transplantation-associated cancers is to specifically prime CD8+ T-cells to recognize the E7 protein of HPV types 5, 8,15 and 16 (Figure 1). Once primed, these cytotoxic CD8+ T-cells will recognize, attack, and kill HPV-infected cells, both pre-neoplastic and cancerous.

Senior cancer researchers at the Cleveland Clinic and University Hospitals Cleveland Medical Center have evaluated FlowVax published data and have joined the team to help take the FlowVax-HPV cancer immunotherapy into clinical testing for organ transplant recipients who have HPV-positive cancers.

The FlowVax-HPV cancer immunotherapy has been developed through Technology Readiness Level (TRL) 6 (platform proof of concept efficacy and safety demonstrated in laboratory animals). The adjuvanted microsphere peptide vaccine platform has been tested in multiple animal models. Peer reviewed journal articles describing the vaccine platform design and showing efficacy for protection against viral challenge have been published (1-3). A full-scale manufacturing process for FlowVax has been developed in Cleveland, Ohio.

Value Proposition

The development and deployment of FlowVax HPV is likely to benefit the entire transplant population. Based on this data we would expect a high acceptance rate for FlowVax HPV which targets HPV strains responsible for skin cancer not targeted by currently marketed HPV vaccines.

There were about 46,000 solid organ transplants in the United States during 2023. If we very conservatively expect 10% penetration at launch this would be 4,600 doses in the US. At $300 USD / dose this translates to $1.4M USD for the first year with expected year over year growth there after.

About the research

(1) Rubsamen RM, Herst CV, Lloyd PM, Heckerman DE, Eliciting cytotoxic T-Lymphocyte Responses from Synthetic Vectors Containing one or two Epitopes in a C57BL/6 Mouse Model Using Peptide-Containing Biodegradable Microspheres and Adjuvants, Vaccine, 2014;33: 4111-4116.

(2) C.V. Herst, S. Burkholz, J. Sidney, A. Sette, P.E. Harris, S. Massey, T. Brasel, E. Cunha- Neto, D.S. Rosa, W.C.H. Chao, R. Carback, T. Hodge, L. Wang, S. Ciotlos, P. Lloyd, R. Rubsamen, An Effective CTL Peptide Vaccine for Ebola Zaire Based on Survivors' CD8+Targeting of a Particular Nucleocapsid Protein Epitope with Potential Implications for COVID-19 Vaccine Design; Vaccine June 9, 2020; 9; 38(28); 4464-4475

(3) Harris PE, Brasel T, Massey C, Herst CV, Burkholz S, Lloyd P, Blankenberg T, Bey TM, Carback R, Hodge T, Ciotlos S, Wang L, Comer JE, Rubsamen RM. A Synthetic Peptide CTL Vaccine Targeting Nucleocapsid Confers Protection from SARS-CoV-2 Challenge in Rhesus Macaques. Vaccines (Basel). 2021 May 18;9(5):520