

Abstract- non-technical- A Pilot Study of Concurrent Docetaxel and a Pox-Vaccine Versus Vaccine Followed by Docetaxel in Metastatic Androgen Independent Prostate Cancer

The treatment of choice for patients with prostate cancer that has spread to other parts of the body (metastasis) is hormonal therapy. However, it is unclear what the best therapy to use for patients who fail such therapy with progression of their disease (androgen independent prostate cancer or AIPC). A number of different chemotherapy drugs have been used with patients with AIPC. Historically, none of these older drug regimens have shown to increase survival in this patient population. A newer chemotherapy agent, docetaxel when given as a weekly injection, has been shown to have activity against AIPC. However, most patients who initially respond to this therapy alone will eventually die with disease progression.

We have previously shown that vaccines can be created against a number of different targets expressed on cancer cells that can be used for therapy against those cancers. PSA is one such target, overexpressed on prostate cancer and rarely expressed on normal tissues. Thus it makes an attractive target for immune therapy. However, we know from our experience that directly injecting PSA protein into a cancer patient produces little if no antitumor activity. Our goal is devising vaccine strategies for prostate cancer is to activate T-cell responses to PSA to a new threshold, which in turn may translate into anticancer activity. These strategies consist of the following: a) Using pox viral vectors containing the gene for PSA which can deliver our target to the immune system in a very efficient manner and increase the immune responses to the target (vaccinia and fowlpox). b) Diversified Prime and Boost – in which we use two different delivery vectors containing PSA which we have previously shown to produce increases in immune responses against that target (1 vaccination priming with vaccinia followed by multiple fowlpox vaccine boosts), c) T-cell costimulation-necessary to activate specific T cells which are necessary to destroy tumor cells (B7. 1), and d) cytokines as biologic adjuvants – helps the immune system amplify responses against the tumor target. Moreover, we have developed an assay to measure immune responses, Elispot assay which allows us to determine if patients receiving the vaccines are mounting increases in immune responses specifically against our target, PSA. The proposed vaccine strategy in this study is currently being used in two ongoing Phase II NC1 clinical trials. Over 40 patients have been vaccinated without any significant side effects. Furthermore, there is preliminary data to suggest there may be clinical responses in some patients receiving the vaccines with decreases in their PSA values that had previously been rising.

In this proposed studies, patients will receive the same vaccine strategy used in the above two ongoing trials. In addition patients on one arm will receive docetaxel 30 mg/m<sup>2</sup>, repeated in 28-day cycles, comprising weekly treatments for three consecutive weeks followed by one week off. Patients who progress on the vaccine alone will commence docetaxel alone using the same schedule. This is a small pilot study, which explores the impact of the addition of docetaxel chemotherapy to a vaccine regimen using the ELISPOT assay. Based on the preclinical activity of taxane/vaccine combinations if a robust immunologic response is seen with the combination of both therapies in this pilot, we will follow this trial with a larger study using clinical endpoints.