

2.7 Rationale for the Use of Leuvectin in Patients Undergoing Radical Prostatectomy and With Prostate Cancer Who Have Failed Radiation Therapy

There is no curative therapy for prostate cancer once it has escaped the confines of the prostate capsule. While surgical therapy offers excellent chances for cure if the disease is pathologically confined to the gland, up to 40% of patients who are considered candidates for radical prostatectomy will have positive margins, capsular penetration, seminal vesicle involvement, or nodal disease which are all adverse prognostic factors for disease recurrence after radical prostatectomy (17). Adjuvant radiotherapy has had varying rates of success when used in the adjuvant setting, and neoadjuvant hormone deprivation therapy cannot preoperatively downstage a prostate cancer to improve rates of organ confined disease (18). Once prostate cancer has spread, androgen deprivation therapy is very effective in controlling symptoms from metastasis, and for slowing the rate of disease growth. However, androgen deprivation treatment is not curative, with the majority of patients eventually developing hormone-refractory disease. Due to the slow rate of prostate cancer cell reproduction, the use of cytotoxic chemotherapy is ineffective since such treatment relies on the selective killing of actively and rapidly

proliferating cells. Immunotherapy offers a different approach to treating the patient with prostate cancer. It is hoped that the animal studies looking at the efficacy of IL-2 based tumor vaccines will translate into efficacy in human studies. By using intratumoral injection of Leuvectin, a cellular immune reaction could be generated against prostate cancer cells without the need to surgically harvest the tumor and grow it in cell culture in the presence of recombinant cytokine. By generating an antitumor response against prostate cancer prior to radical prostatectomy, it is hoped that the enhanced anti-tumor effect generated by treatment will result in improved outcome. It is possible that locally activated antitumor lymphocytes will gain access to the circulation, and that these activated immune cells will detect and destroy micrometastases that otherwise would have escaped immune surveillance. By performing injections prior to radical prostatectomy, we also hope to study the cellular and molecular changes that occur in the prostate after local IL-2 stimulation, with this knowledge eventually leading to a better understanding of the immune response against prostate cancer. The effect of local IL-2 production on human prostate cancer *in vivo* is unknown, and the mechanisms by which prostate cancer escapes immune surveillance is also unknown. However, there is significant potential therapeutic benefit for an IL-2 gene tumor vaccine therapy based on prior *ex vivo* and animal studies.

The treatment options available to patients who failed radiation therapy for prostate cancer are limited. While cryotherapy and salvage prostatectomy offer potential cures for selected patients who have biopsy proven local failure following radiation treatment, the salvage treatments have been associated with low cure rates and high complication rates. For most patients who have rising PSA levels following radiation treatment, the only option is anti-androgen treatment to slow the rate of cancer growth and to palliate symptoms.

3.0 OBJECTIVES

The objectives of this Phase I study include:

- 3.1 To investigate the toxicity of intratumoral injection of Leuvectin in patients with prostate cancer who are scheduled to undergo radical prostatectomy, and in patients who have local recurrence of prostate cancer following radiation therapy. See Appendix A for the clinical and pathologic staging systems for prostate cancer.
- 3.2 To examine the immunologic impact Leuvectin has on prostate cancer cells, and on the local immune system environment.
- 3.3 To evaluate the antitumor activity of Leuvectin based on post-operative pathologic margins, PSA, and disease status following surgery.