

## Points to Consider

### A PHASE I STUDY OF AUTOLOGOUS HUMAN INTERLEUKIN 2 GENE MODIFIED TUMOR CELLS IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC PROSTATE CANCER

#### POINTS TO CONSIDER

##### Part I: Description of Proposal

###### Part I-A: Objectives and rationale of the proposed research.

This is a phase I trial of active immunotherapy using injections of irradiated human IL-2 gene transduced prostate cancer cells (gene modified tumor cells or GMT) in patients with advanced prostate cancer. The NIH-RAC has previously approved the pMP6A/IL-2 vector containing the human IL-2 gene in our Phase I protocol for breast carcinoma in Protocol # 9403-086. Only the target cell for genetic modification *ex vivo* -- autologous prostate cancer cells -- has changed. Three doses of lethally irradiated, autologous prostate cancer cells expanded in short-term culture and transduced with the human IL-2 gene will be tested to determine the highest safely tolerated dose defined by AIS Toxicity Criteria. IL-2 cytokine gene transduced tumor vaccines have potent, long-lasting anti-tumor activity in pre clinical models of melanoma, sarcoma, renal cancer, lung cancer and colon cancer (See review Gilboa and Lyerly). IL-2 gene transduced, irradiated prostate cancer vaccines can cure animals with pre-established hormone resistant, chemotherapy resistant prostate cancer (See Vieweg et. al. Cancer Res.).

Both the active immunotherapy cell dose and IL-2 secretion rate to be evaluated in the Phase I study have published, pre clinical anti tumor efficacy against prostate cancer tumors. Without IL-2 gene transduction, human prostate cancer cells do not secrete IL-2 in vitro. The cell dose ranges tested ( $5 \times 10^6$  -  $5 \times 10^7$ ) and IL-2 secretion rate set in this Phase I study are in the range that have published efficacy in pre clinical testing. The high dose level ( $5 \times 10^7$  cells injected x 4) represents the upper limits of cancer cell yield from prostate cancer removal at radical prostatectomy. If Phase I testing shows safety, a Phase II study will test efficacy with a dose chosen from the Phase I study. Specific objectives of the Phase I study are:

- 1) To evaluate the safety of skin injections of cultured, lethally-irradiated, autologous IL-2 gene transduced prostate cancer cells secreting IL-2 at 10-100 ng/10<sup>6</sup> gene modified tumor cells/24 hrs
- 2) To describe and quantitative the acute toxicities, if any, of irradiated IL-2 gene transduced prostate cancer cell active immune therapy
- 3) To test for induced anti tumor immune responses following therapy.