

## Scientific Abstract

Ovarian cancer accounts for approximately 12,000 deaths per year. Many patients who die of this disease have tumor which is confined to the peritoneal cavity. These patients' tumor cells are resistant to chemotherapy and radiation. New biotechnologies have emerged over the past several years which may provide a novel therapeutic modality for patients with ovarian cancer. We have designed a study that uses an allogeneic genetically modified tumor cell line to inhibit or eradicate preexisting *in situ* tumor cells. This will be accomplished by injecting the irradiated genetically modified tumor cells into the peritoneal cavity of patients with subsequent treatment with the drug ganciclovir.

Preclinical studies have demonstrated the utility of this approach. We have demonstrated that tumor cells containing the herpes simplex thymidine kinase gene (TK) can be killed with the drug ganciclovir (GCV). When TK positive and TK negative tumor cells are mixed in culture and exposed to ganciclovir, all cells can be eradicated even if as few as 10% of the population is TK positive. Thus TK positive cells have a killing effect on the TK negative cells. *In vivo* murine studies demonstrated similar results. We showed that a mixture of TK positive and TK negative tumor cells injected subcutaneously could be eradicated when the animals were treated with ganciclovir. This study was extended to a murine model in which mice had preexisting intraperitoneal tumor cells. We demonstrated that the injection of irradiated TK positive cells with subsequent ganciclovir therapy could prolong animal survival. We further demonstrated that the I.P. injection of irradiated TK positive human tumor cells into mice with a preexisting tumor resulted in cure of approximately 20% of the mice.

We have designed a phase I study to begin to apply the above described preclinical studies to patients with ovarian cancer. Our studies primary objective is to evaluate the safety and side effects of treatment of ovarian cancer patients with an allogeneic gene-modified cancer vaccine which is administered intraperitoneally and activated by ganciclovir.