

I. SCIENTIFIC ABSTRACT

This study will evaluate the safety and efficacy of *in vivo* gene transfer of the Herpes Simplex-thymidine kinase (HStk) gene using PA317/LTKOSN.2 vector producing cells (VPC) in patients with recurrent or refractory ovarian cancer. Insertion of the HStk gene into tumor cells confers a sensitivity to the anti-herpes drug ganciclovir (GCV). The HStk/GCV system induces a bystander effect and an anti-tumor immune response. HStk VPC have destroyed intraperitoneal tumors growing in animals. This selective destruction of growing tumors *in situ* is thought to result from the production of toxic GCV metabolites within the tumor. This procedure has resulted in the cure of experimental animals with limited toxicity. Therefore, we propose to apply this technique for the treatment of refractory or relapsed ovarian cancer.

Adult women (≥ 18 years) with recurrent or refractory ovarian cancer, will be evaluated for the extent and location(s) of their disease before being entered into the study. Patients will have a CT scan and peritonoscopy with biopsy to confirm the diagnosis. During peritonoscopy, eligible patients will have a Tenckhoff catheter placed. HStk VPC will be infused into the peritoneal space. Two weeks later, GCV will be administered at 5 mg/kg/dose IV b.i.d. for 14 days. Patients will only receive one cycle of therapy in this dose escalation protocol. After the completion of the course of GCV, the patient will then be followed at least every 4 weeks for the first 6 months and then at 2 to 6 month intervals. This protocol is related in principle to RAC approved protocols for the treatment of brain tumors in adults and children. This protocol is novel in the site of administration of the HStk VPC and the dose escalation schema.