

MI-2. Non-Technical Abstract. Colorectal cancer is one of the leading causes of cancer deaths in the United States. The major problem is metastatic disease, with liver being the primary site of the metastasis. Liver metastases are clumps of tumor cells which grow within the liver. Tumors cause symptoms and liver dysfunction when the tumor replaces normal functioning liver. Most therapies for colorectal cancer metastases of the liver are directed to limiting the growth of these tumors, and if possible, removing them entirely. The therapies available include chemotherapy, surgery for removal of the metastases, or surgery for the placement of a catheter into an artery in the liver for regional chemotherapy. The basis for this protocol is to transfer a foreign gene, cytosine deaminase (CD), into the cancer cells within the liver. A modified adenovirus, a common cold virus is used to transfer this gene. The modified virus to be used is called Ad_{Gv}CD.10. It is a laboratory-altered virus that can infect cancer cells like a "cold" virus does in the nose, but unlike a "cold" virus, cannot reproduce itself. Ad_{Gv}CD.10 has had inserted into it a gene used to produce the CD enzyme. This enzyme is found in bacteria and fungi, but not found in human cells. The adenovirus "vector" allows the transfer of the CD gene directly to cancer cells. Once inside the cancer cells, this gene directs the production of the CD protein within the cancer cells, allowing these cells to convert the nontoxic antibiotic 5-fluorocytosine (5FC) to the active chemotherapeutic agent 5-fluorouracil (5FU) thereby suppressing their growth. The protocol is designed to evaluate 18 individuals in search of answers to the following important questions regarding gene therapy for liver cancer: (1) Is it safe to administer the modified adenovirus, Ad_{Gv}CD.10 to tumor nodules within the liver?; (2) Will transfer of the CD gene to the tumors enable the tumor cells to produce the CD enzyme?; (3) Will combination of the administration of Ad_{Gv}CD.10 and the administration of the 5FC lead to production of the active, toxic chemotherapeutic agent 5FU within the tumor and will this lead to tumor cell death in the tumor nodule?; (4) Is there evidence reduction of tumor mass or limitation of tumor growth compared to an equal sized tumor nodule not treated?; (5) Does the body develop immunity against Ad_{Gv}CD.10 that will prevent subsequent administrations, i.e., will the body react against the modified virus to prevent it from transferring the normal gene to the tumor should additional administrations be necessary?