

Non-Scientific Abstract

Lay Abstract:

Advanced extremity melanoma is a significant problem, as it is difficult to treat, can be quite disfiguring, and is a significant source of discomfort and diminished quality of life for affected patients. Isolated limb infusion (ILI) is a treatment option for these patients that results in significant response rates; however, this treatment is not curative.

Virotherapy is a treatment for cancer in which viruses are modified to selectively target and kill tumor cells with a low side-effect profile. This approach has been limited by two-main problems - liver damage from the virus and patient anti-viral immune responses. The immune response is how the body recognizes and defends itself against bacteria, viruses, and substances that appear foreign and harmful. We hypothesize that by applying virotherapy via ILI, we will overcome these two limitations of virotherapy.

In this trial, we propose to deliver a melanoma-specific virus via ILI for the treatment of advanced extremity melanoma. ILI is undertaken by selectively isolating the artery and vein of the affected limb, delivering high doses of chemotherapy to the limb via the artery, followed by removal of the chemotherapy via the vein, thereby minimizing overall side effects and directly delivering chemotherapy to the patient's tumor. We believe that this method of delivery is an optimal system for the application of tumor directed virotherapy. Patients treated in this trial will receive virus via the ILI system, limiting possible liver side effects. Additionally, patients will receive one dose of viral therapy, circumventing the possible anti-virus immunity developed by patients. The virus utilized in this trial has previously been used as a locally-directed therapy in patients with cancer and has been shown to be safe in humans.

In summary, we propose to apply a tumor-specific virus via a local delivery mechanism (isolated limb infusion) for the treatment of advanced extremity melanoma. This represents the utilization of a novel therapeutic modality via an optimal delivery mechanism in a patient group with few treatment options.