Technical Abstract

This investigation will examine the safety and efficacy of using an adenoviral vector to deliver the herpes thymidine kinase gene (AdV/RSV-TK) directly into the tumor followed by oral administration of valganciclovir for the treatment of patients with retinoblastoma. This protocol also allows for re-treatment of patients who have been previously treated with AdV/RSV-TK and valganciclovir or ganciclovir.

Retinoblastoma is the most common primary malignant tumor of children and usually occurs in children under the age of 3 years. Current standard treatment for nonmetastatic retinoblastoma is enucleation. Although this results in a high rate of survival, enucleation results in blindness and severe cosmetic facial deformity. Recently, attention has been turned to finding alternative therapies that will result in a high cure rate but will allow salvage of the affected eye. Occasionally a child presents with a small tumor that can be eradicated with cryotherapy or laser photocoagulation while still preserving the eye and useful vision. Unfortunately, most children present with tumors that are too large for these types of therapies. In an attempt to shrink a larger tumor to a size that can be managed by these local therapies, clinical investigators have begun trials using systemic chemotherapy and/or radiation therapy instead of enucleation. Although preliminary studies have shown promise, these therapies have significant side effects including an increased rate of second malignancies. Because patients with retinoblastoma have a significant second malignancy potential, an alternative therapy without systemic toxicity would be desirable.

We have previously found in a phase I clinical trial that vitreous seeds in children with retinoblastoma could safely be treated with an adenoviral vector delivering the herpes thymidine kinase gene (AdV/RSV-TK) followed by intravenous ganciclovir and that these vitreous seeds have responded to the treatment. Based on this data, we propose to test the safety and efficacy of this treatment when administered directly into tumors of patients with retinoblastoma not complicated by vitreous seeds. This protocol is designed to reduce the size of tumors so standard therapies can be employed to treat any remaining disease and salvage the eye.