

Non-technical Abstract

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.

The presence of vitreous tumor seeds has been particularly difficult to treat and usually predicts treatment failure prompting enucleation. In recent years, an increased emphasis has been placed on finding therapies for retinoblastoma that allow for the salvage of the affected eye even to the extent of using potentially toxic therapeutic regimens such as systemic chemotherapy and radiotherapy. There is a need to develop new and innovative therapies that will salvage the eye while still curing children with retinoblastoma without systemic toxicity.

In a phase I study previously undertaken using this AdV/RSV-TK gene transfer approach in children with vitreous seeds associated with retinoblastoma, none of the patients developed gene transfer-related toxicities that were indications for enucleation and no dose-limiting toxicities were observed. The goal of this study is to expand on knowledge gained from the phase I study to further evaluate the safety and efficacy of this treatment in patients with retinoblastoma complicated by vitreous seeds.