A Systematic Review of Oncolytic Viruses and Gene Therapies for Retinoblastoma in Children

HTA24

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SUMMARY

OBJECTIVES

- Retinoblastoma is a rare cancer of the eye which primarily affects children. It can lead to varying degrees of vision loss, and in some cases surgical removal of the affected eye(s) is required, which can negatively impact patients' quality of life.
- Oncolytic viruses and gene therapies are novel, experimental treatments being investigated for use across several oncological indications, but there is uncertainty surrounding their efficacy and safety.
- A systematic literature review was conducted to evaluate published efficacy and safety data from clinical trials of oncolytic viruses and gene therapies in children with retinoblastoma.

METHODS

- Comprehensive searching of electronic databases and supplementary sources was conducted.
- Trials that investigated oncolytic viruses and gene therapies for childhood retinoblastoma and were published on or before 7th January 2026, were included.
- Cochrane and PRISMA guidelines for SLRs were followed.
- The study protocol was registered (PROSPERO: CRD420251064061).

FINDINGS

- In total, 8 publications reporting on two phase I, high-risk of bias clinical trials were identified.
- In one study, targeted vitreous seeds were resolved in all 8 children treated intravitreally with adenoviral vectors containing a herpes thymidine kinase gene followed by intravenous ganciclovir, however, all patients were eventually enucleated.
- A second study reported partial responses in 5/9 children with retinoblastoma treated with the oncolytic adenovirus VCN-01. 6 children were enucleated, and vision was preserved in 3 eyes at follow-up.

CONCLUSIONS

- Published data on the efficacy and safety of oncolytic viruses and gene therapies in children with retinoblastoma is limited. Further clinical studies are needed to validate the findings of Phase I trials.

BACKGROUND & AIMS

- Retinoblastoma is a primarily paediatric, rare, intraocular cancer caused by mutations in the RB1 gene which can lead to mild-to-severe vision loss.
- Pre-clinical and early-phase clinical studies have investigated the viability of oncolytic viruses and gene therapies in targeting the RB1 gene pathway, but there is uncertainty surrounding their efficacy and safety.
- This review aimed to comprehensively identify and describe published data from clinical trials of oncolytic viruses and gene therapies in children with retinoblastoma.

METHODS

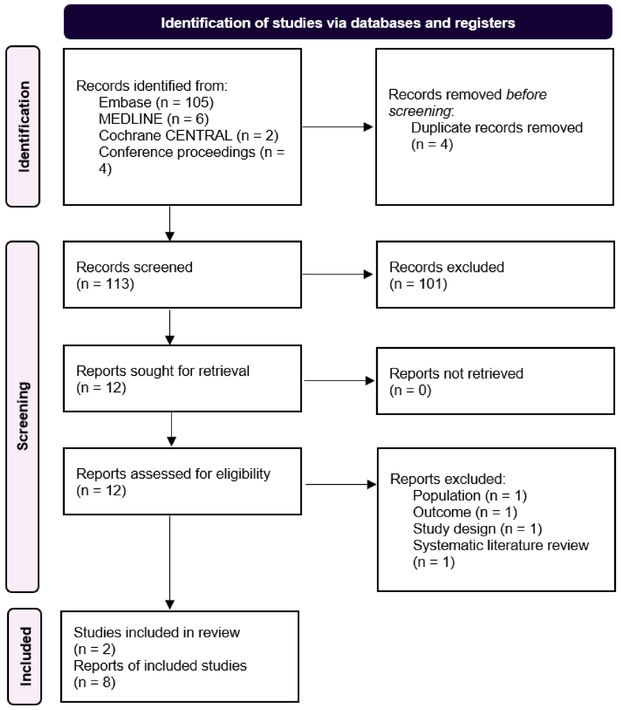
- A PRISMA-adherent systematic literature review,[1] following recommendations from the Cochrane Handbook for Systematic Reviews of Interventions,[2] included electronic database searches on 7th January 2026 of Embase, MEDLINE(R) ALL and the Cochrane Central Register of Controlled Trials (CENTRAL) to identify clinical trials of oncolytic viruses and gene therapies in children diagnosed with retinoblastoma.
- Other resources searched included conference proceedings from the American Society of Clinical Oncology Annual Meeting, the Society of Gene and Cell Therapy Annual Meeting, the European Society for Medical Oncology Annual Meeting, the European Society for Medical Oncology-Asia Annual Meeting, the Japanese Society of Medical Oncology (JSMO) Annual Meeting, the Research in Vision and Ophthalmology Annual Meeting, and the World Cancer Congress. Clinical trial registries including ClinicalTrials.gov, World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and European Union (EU) Clinical Trials Register were also searched. The study protocol was registered with PROSPERO: CRD420251064061.

Table 1. Inclusion and exclusion criteria

Inclusion	Exclusion
Population	
• Children (<18 years) diagnosed with retinoblastoma • Mixed diagnosis populations where results for retinoblastoma patients are reported separately • Mixed age populations where results for children are reported separately	• Adults (≥18y) • Patients without a retinoblastoma diagnosis • Mixed diagnosis populations where results for retinoblastoma patients are not reported separately • Mixed age populations where results for children are not reported separately (unlikely as retinoblastoma is a childhood cancer)
Intervention	
• Oncolytic viral therapies • Gene therapies	• Surgical interventions where not used in combination with included interventions • Chemotherapy where not used in combination with included interventions
Comparator	
• Any	• N/A
Outcomes	
Include	**Exclude**
• Response rates • Progression-free survival • Surgery/enucleation rates • Vision loss • HRQoL • Adverse events	• Non-clinical outcomes (e.g. economic evaluations)
Study design	
• Clinical trials (all phase) • Systematic reviews (for reference checking only)	• Retrospective and prospective observational studies (e.g. cohort, case-control) • Case series/case reports • Non-systematic reviews • Editorials, letters, comments, etc.

- Two reviewers independently screened records for inclusion according to prespecified criteria (Table 1) at title/abstract and full text stage, performed data extraction and risk of bias assessments. Any discrepancies between reviewers were resolved through consensus or third reviewer adjudication.
- Extracted data items included study details, patient characteristics, and clinical and safety outcomes.
- Risk of bias of included trials was assessed using the Cochrane ROBINS-I tool.

Figure 1. PRISMA flow diagram



RESULTS

- Of 117 records identified through database and supplementary searches, 8 publications reporting on 2 unique clinical studies of oncolytic viruses and gene therapies in children diagnosed with retinoblastoma were selected for inclusion within this review (Figure 1).[3-10]
- Both included studies were phase I, single-arm trials, with patient populations consisting of children with previously treated retinoblastoma.
- In one study (Chévez-Barrios (2005)), refractory retinoblastoma patients were treated intravitreally with adenoviral vectors containing a herpes thymidine kinase gene followed by intravenous ganciclovir. Targeted vitreous seeds were resolved in all 8 children who were treated, however, toxicities such as inflammation, corneal oedema, and increased intraocular pressure were observed, and all patients were eventually enucleated.[3-8]
- The second study (NCT03284268) investigated the use of the oncolytic adenovirus VCN-01 in retinoblastoma patients who had failed previous therapy. Partial responses were observed in 5/9 children treated. Adverse events were observed in 7 patients, with uveitis being the most frequently reported. Six children were enucleated, and vision was preserved in 3 eyes at follow-up (12-49 months).[9-10]
- Both studies were evaluated as being of serious risk of bias according to the Cochrane ROBINS-I tool. This was primarily due to a critical risk of bias in the confounding domain as both studies were single-arm in design.

Table 2. Included studies

Study	Phase	Patient population	Intervention	Study size
NCT03284268[9-10]	Phase I	Children aged between 1-12 years with intraocular retinoblastoma who failed conservative therapy facing imminent enucleation	VCN-01	13 enrolled, 9 treated
Chévez-Barrios (2005)[3-8]	Phase I	Children with bilateral retinoblastoma who had previously failed conventional therapy	AdV/TK followed by systemic administration of ganciclovir	8 enrolled and treated

CONCLUSIONS

- Although oncolytic viruses and gene therapies are regarded as experimental in children with retinoblastoma, early clinical trials have demonstrated their potential efficacy and safety for intraocular use.
- Only single-arm, phase I clinical trials were identified in this review. Therefore, the efficacy and safety of oncolytic viruses and gene therapies in comparison to current standard-of-care therapies (e.g. chemotherapy) and surgical interventions is unclear. Larger, long-term controlled studies are needed to further validate Phase I results and address this research gap.
- Both studies included in this review had previously treated patient populations, so it is unclear as to what the efficacy and safety of oncolytic viruses and gene therapies in untreated retinoblastoma patients may be. Further clinical studies of these therapies in newly diagnosed patients are needed to address this knowledge gap.

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