Oncolytic Adenoviral Treatment of Brain Tumors: A Scoping Review Protocol

Registration

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Abstract

Background:
Oncolytic virotherapy (OVT) is a relatively new tool in the armament of cancer treatment choices. One of the vectors used is the adenovirus (AdV); it has been well-studied in OVT.[1-4] Through genetic modification, AdVs are adept at targeting tumor cells, causing tumor cell death. These cells then release cytokines that recruit immune cells and amplify the immune response to cancer while continuing to infect adjacent tumor cells due to innate properties of viral replication that are also enhanced by genetic modification.[1, 3] It has also been found that the use of AdV OVT can be used in conjunction with other anti-cancer therapies without added toxicities.[3] In our scoping review, we aim to collect the global literature on adenoviral OVT in the treatment of primary brain cancer – a type of solid cancer - and synthesize the key qualitative and quantitative findings from the included articles.

Objectives: This scoping review study aims to identify the types of brain tumors that are being treated with adenoviral oncolytic viral therapy (OVT) as well as the corresponding quantitative and qualitative patient outcomes determined by the included articles. We also hope to identify any gaps in the literature including a lack of research in certain populations, for example.

Methods:
We will be following the PRISMA-Scr guidelines proposed by Arksey and O'Malley to adapt the PRISMA systematic review guidelines to our broader research question.

Amendments:
Any relevant protocol changes will be documented with date, description, and reasoning for change as needed throughout the study.

1) Identification of Research Questions:

Primary questions:

- What types of brain cancer in humans is AdV OVT being used to treat?
- What are the targets of AdV OVT in brain cancer?

Sub-questions:

- What adenoviral OVT is being used in pediatric populations with brain tumors?
- What treatments are being used in conjunction with oncolytic adenoviral treatments?

Methods

We modeled our protocol after that proposed by Heinemann et al. following the Arksey and O'Malley scoping review protocol.[5, 6] Moher et al. provides a seven-step process to guide the development of a high-quality systematic review named the preferred reporting items for systematic reviews and meta-analysis (PRISMA)[7] which has been adapted by the Joanna Briggs Institute (JBI) for scoping reviews, the PRISMA-ScR.[8-10] The PRISMA-ScR checklist will be used to maintain the methodological rigor of the review.[9] Comprehensive searches of published and gray literature will be conducted on various global electronic databases to seek adenoviral OVT use in clinical settings for the treatment of brain cancer. Pairs of independent reviewers will perform eligibility decisions using Rayyan, a free online article screening tool.[11] Data from selected studies will be extracted and analyzed by the research team. Information related to AdV OVT use in primary brain cancer will be synthesized to develop a list of types of articles eligible for inclusion, to determine the specific types of brain cancer, age groupings of treatment recipients, and the types of treatments used in conjunction with adenoviral OVT as well as to provide a narrative synthesis of results.

Contributions

VJH is the lead of protocol development with mentorship and assistance from ABW and MD. Pairs of reviewers will research the titles and abstracts for inclusion. ABW is the research librarian assisting with search strategy formulation with VJH. VJH, KA, GB, BG, MJ, AK, RW, and MD will perform article eligibility, data abstraction, and synthesis. All listed contributors will contribute to the interpretation of data, manuscript writing, and approval of the final manuscript.

Eligibility Criteria:

Study eligibility and inclusion will be based on the criteria listed below.

Inclusion:

- Type of article: clinical trials, case studies, case series whose primary focus is on the use of adenoviral OVT in the treatment of primary brain tumors
- Publication date: between the start of database collection to 2023
- Language: English
- Populations: human subjects of all ages with primary brain tumors

Exclusion:

- Type of article: in vitro studies, editorials, legal analysis/opinions, introductions, study protocols, letters to the editors, abstracts
- Language: non-English

- Populations: animal subjects, cell lines, and humans with cancers other than primary brain tumors

Information Sources:
The following bibliographic databases will be used to complete this search:

- The Cochrane Library (Wiley)
- CINAHL Plus with Full Text (Ebsco)
- Pubmed (Ovid)
- Embase
- Scopus (Elsevier)
- ProQuest dissertations & Theses Global

Search Strategy
The review authors will collaborate with a research librarian (ABW) to create a comprehensive search for the concepts of oncolytic adenovirus therapy and brain tumors. The search will combine both title/abstract keywords and database-specific controlled vocabulary. The following databases will be searched from inception to present without the use of filters or limits: MEDLINE (PubMed), Cochrane Library, Embase (Elsevier), CINAHL (Ebsco), Scopus (Elsevier), and ProQuest Dissertations and Theses Global. The results will be imported to a citation management software (EndNote) where they will undergo multi-pass deduplication. Unique records will be uploaded to a screening platform (Rayyan) for a blinded title/abstract screening by a minimum of two reviewers.

Examples of our search strings are listed in Appendix A.

Study Records
Study citations will be managed with EndNote.[12] Selected abstracts and full-text manuscripts will be accessible by the reviewers based on the citation list created. Rayyan will be used to manage titles and abstracts and ultimately assist with literature selection and data extraction.[7]

Selection Process
After a pilot training period of collective review of 100 abstracts to confirm reviewers understand the inclusion and exclusion criteria, pairs of independent reviewers will screen the article titles and abstracts that were obtained through the above-listed search strategy for eligibility using Rayyan, a free online tool designed by Ouzzani et al. for systematic reviews and those projects synthesizing knowledge, like this scoping review.[6] If the abstract or title lack sufficient information to determine inclusion or exclusion, the full text will be accessed to assess for inclusion. Full-text manuscripts will be accessed and reviewed for those studies that meet inclusion criteria, with an agreement between the pairs of reviewers. The research team will evaluate articles if disagreement exists between the pair of reviewers to come to a consensus. Documentation or rationale for the inclusion and exclusion of specific titles, abstracts, and full

texts will be performed. A PRISMA flow diagram will be used to report the final numbers in the resulting numbers in manuscript.[5]

Data Charting Process

The research team will create the initial Excel sheet for data charting based on common results and study characteristics on the initial screening of included articles. Data charting categories will be jointly agreed upon by the screeners to assure the inclusion of key findings. We plan to extract and summarize the following characteristics to the data extraction sheet: (1) research characteristics (type of study); (2) types of brain cancers; (3) treatment population demographics (age, race, gender); (4) types of treatments used in conjunction with this OVT; (5) Method of application of AdV (6) quantitative findings, such as a change in tumor size, length of survival post-treatment (7) qualitative findings, such as treatment-related symptoms and changes in quality of life.

Pairs of reviewers will independently chart the data from each eligible study into Excel. The two reviewers will resolve the disagreement through discussion. If an agreement between the two reviewers is not possible, they may include a third expert reviewer for the resolution of disagreement and final decision.[8]

Data Synthesis

The interrater reliability, Fleiss' kappa, will be calculated with the Real Statistics Resource Pack on Excel[13] after the initial pilot is completed. Our goal is a kappa >0.8. If this kappa is not attained, disagreements will be settled by discussion between screeners, reaching out to the most senior author, if need be, and the pilot will be re-run with a new set of articles with a subsequent recalculation of Fleiss' kappa. The process will be repeated until a kappa >0.8 is attained or all articles have been reviewed.

Data analysis will be conducted by Analysis ToolPak on Excel to determine the descriptive statistics of the quantitative data found (mean, median, mode, range) with analysis of variance (ANOVA) testing to determine if the means of the populations of each study are equal.[14] We will analyze the combination of therapies applied to tumor types as well as the effectiveness this treatment had on patients as measured by their survival time after treatment. The team will review the analysis for errors.

Implications and Dissemination

We aim to characterize the use of AdV OVTs in the treatment of primary brain tumors and their impact on patient outcomes. We will also investigate any gaps in the literature to promote research in these areas. The study findings will provide insight into the use of AdV OVT more generally in the treatment of brain tumors. The results of the scoping review will be disseminated through a peer-reviewed publication.

Support

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References

1. Chow LT, Gelinas RE, Broker TR, Roberts RJ. An amazing sequence arrangement at the 5' ends of adenovirus 2 messenger RNA. *Cell*. Sep 1977;12(1):1-8. doi:10.1016/0092-8674(77)90180-5
2. Tanoue K, Rosewell Shaw A, Watanabe N, et al. Armed Oncolytic Adenovirus-Expressing PD-L1 Mini-Body Enhances Antitumor Effects of Chimeric Antigen Receptor T Cells in Solid Tumors. *Cancer Res*. Apr 15 2017;77(8):2040-2051. doi:10.1158/0008-5472.can-16-1577
3. Mantwill K, Klein FG, Wang D, et al. Concepts in Oncolytic Adenovirus Therapy. *Int J Mol Sci*. Sep 29 2021;22(19)doi:10.3390/ijms221910522
4. Kovesdi I, Reichel R, Nevins JR. Identification of a cellular transcription factor involved in E1A trans-activation. *Cell*. Apr 25 1986;45(2):219-28. doi:10.1016/0092-8674(86)90386-7
5. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology*. 2005/02/01 2005;8(1):19-32. doi:10.1080/1364557032000119616
6. Heinemann A, Wafford QE, Pedersen JP, et al. Service-delivery competencies of workers delivering Home and Community Based Services (HCBS): a scoping review. 2020
7. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. Aug 18 2009;151(4):264-9, W64. doi:10.7326/0003-4819-151-4-200908180-00135
8. Peters M, Godfrey C, McInerney P, Soares C, Khalil H, Parker D. Methodology for JBI Scoping Reviews. 2015:1-24.
9. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med*. Oct 2 2018;169(7):467-473. doi:10.7326/M18-0850
10. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc*. Sep 2015;13(3):141-6. doi:10.1097/XEB.0000000000000050
11. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*. Dec 5 2016;5(1):210. doi:10.1186/s13643-016-0384-4
12. *EndNote*. Version EndNote 20. Clarivate; 2013.
13. *Real Statistics Using Excel*. Version 8.5 Excel 2010/2013/2016/2019/2021/365 Windows. 2013. Accessed 3 March 2023. https://real-statistics.com/
14. *Excel Analysis ToolPak*. Version Excel for Microsoft 365. https://www.excel-easy.com/data-analysis/analysis-toolpak.html

Appendix A: Database Search Strings

Table 1. PubMed Medline search string.

Search	Hits
(("Oncolytic Virotherapy"[Mesh] OR Oncolytic-viral*[tiab] OR Oncolytic-Virotherap*[tiab] OR Oncolytic-Virus-Therap*[tiab] OR Oncolytic-virus*[tiab] OR Oncorine[tiab] OR OVT[tiab] OR RIGVIR[tiab] OR T-VEC[tiab]) AND ("adenoviridae"[MeSH Terms] OR adenovirus*[tiab] OR adenoviridae[tiab] OR adenoviral*[tiab]) OR (Oncolytic-adenovirus*[tiab] OR oncolytic-adenoviral*[tiab] OR ICOVIR17[tiab] OR oAds[tiab])) AND ("Brain Neoplasms"[Mesh] OR "Glioma"[Mesh] OR "Neoplasms, Germ Cell and Embryonal"[Mesh] OR Anaplastic-oligodendroglioma*[tiab] OR Astrocytoma[tiab] OR ATRT[tiab] OR Atypical-Teratoid-Rhabdoid-Tumor*[tiab] OR Atypical-Teratoid-Rhabdoid-Tumour*[tiab] OR brain-cancer*[tiab] OR brain-neoplasm*[tiab] OR Brain-tumor*[tiab] OR Brain-tumour*[tiab] OR Chondroma*[tiab] OR Chordoma*[tiab] OR Choroid-plexus-carcinoma*[tiab] OR Choroid-plexus-papilloma*[tiab] OR Choroid-plexus-tumors[tiab] OR Craniopharyngioma*[tiab] OR Diffuse-intrinsic-pontine[tiab] OR DIPG[tiab] OR DNT[tiab] OR Ependymoblastoma*[tiab] OR ependymoma[tiab] OR Ependymoma*[tiab] OR Ganglioglioma[tiab] OR GBM[tiab] OR GCT[tiab] OR germ-cell-tumor*[tiab] OR germ-cell-tumour*[tiab] OR Germinoma*[tiab] OR glioblastoma*[tiab] OR Glioma[tiab] OR Gliomatosis-cerebri[tiab] OR Gliosarcoma[tiab] OR Hamartoma*[tiab] OR Hemangioblastoma*[tiab] OR Lipoma*[tiab] OR Medulloblastoma*[tiab] OR Meningioma*[tiab] OR Neurocytoma*[tiab] OR Neurofibroma*[tiab] OR Neuroma*[tiab] OR oligodendroglioma[tiab] OR Pineal-cyst*[tiab] OR Pineal-Tumor*[tiab] OR Pineal-tumour*[tiab] OR Pineoblastoma*[tiab] OR Pineoblastoma*[tiab] OR Pineocytoma*[tiab] OR Pituitary-adenoma*[tiab] OR Pituitary-carcinoma*[tiab] OR Pituitary-tumor*[tiab] OR Pituitary-tumour*[tiab] OR PNET[tiab] OR tumor-of-the-brain[tiab] OR Primitive-neuroectodermal-tumor*[tiab] OR Primitive-neuroectodermal-tumour*[tiab] OR Rathke's-cleft-cyst*[tiab] OR Sarcomas[tiab] OR Schwannoma*[tiab] OR SEGA[tiab] OR SGCA[tiab] OR SGCT[tiab] OR subependymoma[tiab] OR Teratoma*[tiab])	348

Table 2. Cochrane CENTRAL search string.

ID	Search	Hits
#1	MeSH descriptor: [Oncolytic Virotherapy] explode all trees	24
#2	(Oncolytic-viral* OR Oncolytic-Virotherap* OR Oncolytic-Virus-Therap* OR Oncolytic-virus* OR Oncorine OR OVT OR RIGVIR OR T-VEC):ti,ab,kw	142
#3	#1 or #2	142
#4	MeSH descriptor: [adenoviridae] explode all trees	236
#5	(adenovirus* OR adenoviridae OR adenoviral*):ti,ab,kw	1078
#6	#4 or #5	1078
#7	#3 and #6	16
#8	(Oncolytic-adenovirus* OR oncolytic-adenoviral* OR ICOVIR17 OR oAds):ti,ab,kw	480
#9	#7 or #8	489
#10	MeSH descriptor: [Brain Neoplasms] explode all trees	2647
#11	MeSH descriptor: [Glioma] explode all trees	1700
#12	MeSH descriptor: [Neoplasms, Germ Cell and Embryonal] explode all trees	5295
#13	(Anaplastic-oligodendroglioma* OR Astrocytoma OR ATRT OR Atypical-Teratoid-Rhabdoid-Tumor* OR Atypical-Teratoid-Rhabdoid-Tumour* OR brain-cancer* OR brain-neoplasm* OR Brain-tumor* OR Brain-tumour* OR Chondroma* OR Chordoma* OR Choroid-plexus-carcinoma* OR Choroid-plexus-papilloma* OR Choroid-plexus-tumors OR Craniopharyngioma* OR Diffuse-intrinsic-pontine OR DIPG OR DNT OR Ependymoblastoma* OR ependymoma OR Ependymoma* OR Ganglioglioma OR GBM OR GCT OR germ-cell-tumor* OR germ-cell-tumour* OR Germinoma* OR glioblastoma* OR Glioma OR Gliomatosis-cerebri OR Gliosarcoma OR Hamartoma* OR Hemangioblastoma* OR Lipoma* OR Medulloblastoma* OR Meningioma* OR Neurocytoma* OR Neurofibroma* OR Neuroma* OR oligodendroglioma OR Pineal-cyst* OR Pineal-Tumor* OR Pineal-tumour* OR Pineoblastoma* OR Pineoblastoma* OR Pineocytoma* OR Pituitary-adenoma* OR Pituitary-carcinoma* OR Pituitary-tumor* OR Pituitary-tumour* OR PNET OR	9757

	tumor-of-the-brain OR Primitive-neuroectodermal-tumor* OR Primitive-neuroectodermal-tumour* OR Rathke's-cleft-cyst* OR Sarcomas OR Schwannoma* OR SEGA OR SGCA OR SGCT OR subependymoma OR Teratoma*):ti,ab,kw	
#14	#10 or #11 or #12 or #13	13074
#15	#9 AND #14	6

Table 3. Embase search string.

ID	Search	Hits
1	((('oncolytic virotherapy'/exp OR 'oncolytic viral*':ti,ab OR 'oncolytic virotherap*':ti,ab OR 'oncolytic virus therap*':ti,ab OR 'oncolytic virus*':ti,ab OR oncorine:ti,ab OR ovt:ti,ab OR rigvir:ti,ab OR 't vec':ti,ab) AND ('adenoviridae'/exp OR adenovirus*:ti,ab OR adenoviridae:ti,ab OR adenoviral*:ti,ab)) OR ('oncolytic adenovirus*':ti,ab OR 'oncolytic adenoviral*':ti,ab OR icovir17:ti,ab OR oads:ti,ab)) AND ('brain tumor'/exp OR 'glioma'/exp OR 'germ cell and embryonal neoplasms'/exp OR 'anaplastic oligodendroglioma*':ti,ab OR astrocytoma:ti,ab OR atrt:ti,ab OR 'atypical teratoid rhabdoid tumor*':ti,ab OR 'atypical teratoid rhabdoid tumour*':ti,ab OR 'brain cancer*':ti,ab OR 'brain neoplasm*':ti,ab OR 'brain tumor*':ti,ab OR 'brain tumour*':ti,ab OR chondroma*:ti,ab OR chordoma*:ti,ab OR 'choroid plexus carcinoma*':ti,ab OR 'choroid plexus papilloma*':ti,ab OR 'choroid plexus tumors':ti,ab OR craniopharyngioma*:ti,ab OR 'diffuse intrinsic pontine':ti,ab OR dipg:ti,ab OR dnt:ti,ab OR ependymoblastoma*:ti,ab OR ependymoma:ti,ab OR ependymoma*:ti,ab OR ganglioglioma:ti,ab OR gbm:ti,ab OR gct:ti,ab OR 'germ cell tumor*':ti,ab OR 'germ cell tumour*':ti,ab OR germinoma*:ti,ab OR glioblastoma*:ti,ab OR glioma:ti,ab OR 'gliomatosis cerebri':ti,ab OR gliosarcoma:ti,ab OR hamartoma*:ti,ab OR hemangioblastoma*:ti,ab OR lipoma*:ti,ab OR medulloblastoma*:ti,ab OR meningioma*:ti,ab OR neurocytoma*:ti,ab OR neurofibroma*:ti,ab OR neuroma*:ti,ab OR oligodendroglioma:ti,ab OR 'pineal cyst*':ti,ab OR 'pineal tumor*':ti,ab OR 'pineal tumour*':ti,ab OR pineoblastoma*:ti,ab OR pineocytoma*:ti,ab OR 'pituitary adenoma*':ti,ab OR 'pituitary carcinoma*':ti,ab OR 'pituitary tumor*':ti,ab OR 'pituitary tumour*':ti,ab OR pnet:ti,ab OR 'tumor of the brain':ti,ab OR 'primitive neuroectodermal tumor*':ti,ab OR 'primitive neuroectodermal tumour*':ti,ab OR 'rathkes cleft cyst*':ti,ab OR sarcomas:ti,ab OR schwannoma*:ti,ab OR sega:ti,ab OR sgca:ti,ab OR sgct:ti,ab OR subependymoma:ti,ab OR teratoma*:ti,ab)	550

Table 4. CINAHL search string.

ID	Search	Hits
S1	(MH "Oncolytic Virotherapy")	51
S2	TI (Oncolytic-viral* OR Oncolytic-Virotherap* OR Oncolytic-Virus-Therap* OR Oncolytic-virus* OR Oncorine OR OVT OR RIGVIR OR T-VEC) OR AB (Oncolytic-viral* OR Oncolytic-Virotherap* OR Oncolytic-Virus-Therap* OR Oncolytic-virus* OR Oncorine OR OVT OR RIGVIR OR T-VEC)	447
S3	S1 OR S2	450
S4	(MH "Adenoviruses")	126
S5	TI (adenovirus* OR adenoviridae OR adenoviral*) OR AB (adenovirus* OR adenoviridae OR adenoviral*)	2620
S6	S4 OR S5	2651
S7	S3 AND S6	46
S8	TI (Oncolytic-adenovirus OR oncolytic-adenoviral OR ICOVIR17 OR oAds) OR AB (Oncolytic-adenovirus* OR oncolytic-adenoviral* OR ICOVIR17 OR oAds)	478
S9	S7 or S8	493
S10	(MH "Brain Neoplasms+")	17823
S11	(MH "Glioma+")	10700
S12	(MH "Neoplasms, Germ Cell and Embryonal")	1951
S13	TI (anaplastic-oligodendroglioma* OR astrocytoma OR atrt OR atypical-teratoid-rhabdoid-tumor* OR atypical-teratoid-rhabdoid-tumour* OR brain-cancer* OR brain-neoplasm* OR brain-tumor* OR brain-tumour* OR chondroma* OR chordoma* OR choroid-plexus-carcinoma* OR choroid-plexus-papilloma* OR choroid-plexus-tumors OR craniopharyngioma* OR diffuse-intrinsic-pontine OR dipg OR dnt OR ependymoblastoma* OR ependymoma OR ependymoma* OR ganglioglioma OR gbm OR gct OR germ-cell-tumor* OR germ-cell-tumour* OR germinoma* OR glioblastoma* OR glioma OR gliomatosis-cerebri OR gliosarcoma OR hamartoma* OR hemangioblastoma* OR lipoma* OR medulloblastoma* OR meningioma* OR neurocytoma* OR neurofibroma* OR neuroma* OR oligodendroglioma OR pineal-cyst* OR pineal-tumor* OR pineal-tumour* OR pineoblastoma* OR pineoblastoma* OR pineocytoma* OR pituitary-adenoma* OR pituitary-carcinoma* OR pituitary-tumor* OR pituitary-tumour* OR pnet OR tumor-of-the-brain OR	51098

	primitive-neuroectodermal-tumor* OR primitive-neuroectodermal-tumour* OR rathke's-cleft-cyst* OR sarcomas OR schwannoma* OR sega OR sgca OR sgct OR subependymoma OR teratoma*) OR AB (anaplastic-oligodendroglioma* OR astrocytoma OR atrt OR atypical-teratoid-rhabdoid-tumor* OR atypical-teratoid-rhabdoid-tumour* OR brain-cancer* OR brain-neoplasm* OR brain-tumor* OR brain-tumour* OR chondroma* OR chordoma* OR choroid-plexus-carcinoma* OR choroid-plexus-papilloma* OR choroid-plexus-tumors OR craniopharyngioma* OR diffuse-intrinsic-pontine OR dipg OR dnt OR ependymoblastoma* OR ependymoma OR ependymoma* OR ganglioglioma OR gbm OR gct OR germ-cell-tumor* OR germ-cell-tumour* OR germinoma* OR glioblastoma* OR glioma OR gliomatosis-cerebri OR gliosarcoma OR hamartoma* OR hemangioblastoma* OR lipoma* OR medulloblastoma* OR meningioma* OR neurocytoma* OR neurofibroma* OR neuroma* OR oligodendroglioma OR pineal-cyst* OR pineal-tumor* OR pineal-tumour* OR pineoblastoma* OR pineoblastoma* OR pineocytoma* OR pituitary-adenoma* OR pituitary-carcinoma* OR pituitary-tumor* OR pituitary-tumour* OR pnet OR tumor-of-the-brain OR primitive-neuroectodermal-tumor* OR primitive-neuroectodermal-tumour* OR rathke's-cleft-cyst* OR sarcomas OR schwannoma* OR sega OR sgca OR sgct OR subependymoma OR teratoma*)	
S14	S10 OR S11 OR S12 OR S13	60122
S15	S9 AND S14	18

Table 5. Scopus search string.

ID	Search	Hits
1	TITLE-ABS ((oncolytic-viral* OR oncolytic-virotherap* OR oncolytic-virus-therap* OR oncolytic-virus* OR oncorine OR ovt OR rigvir OR t-vec) AND (adenovirus* OR adenoviridae OR adenoviral*)) OR TITLE-ABS (oncolytic-adenovirus* OR oncolytic-adenoviral* OR icovir17 OR oads) AND TITLE-ABS (anaplastic-oligodendroglioma* OR astrocytoma OR atrt OR atypical-teratoid-rhabdoid-tumor* OR atypical-teratoid-rhabdoid-tumour* OR brain-cancer* OR brain-neoplasm* OR brain-tumor* OR brain-tumour* OR chondroma* OR chordoma* OR choroid-plexus-carcinoma* OR choroid-plexus-papilloma* OR choroid-plexus-tumors OR craniopharyngioma* OR diffuse-intrinsic-pontine OR dipg OR dnt OR ependymoblastoma* OR ependymoma OR ependymoma* OR ganglioglioma OR gbm OR gct OR germ-cell-tumor* OR germ-cell-tumour* OR germinoma* OR glioblastoma* OR glioma OR gliomatosis-cerebri OR gliosarcoma OR hamartoma* OR hemangioblastoma* OR lipoma* OR medulloblastoma* OR meningioma* OR neurocytoma* OR neurofibroma* OR neuroma* OR oligodendroglioma OR pineal-cyst* OR pineal-tumor* OR pineal-tumour* OR pineoblastoma* OR pineoblastoma* OR pineocytoma* OR pituitary-adenoma* OR pituitary-carcinoma* OR pituitary-tumor* OR pituitary-tumour* OR pnet OR tumor-of-the-brain OR primitive-neuroectodermal-tumor* OR primitive-neuroectodermal-tumour* OR rathke's-cleft-cyst* OR sarcomas OR schwannoma* OR sega OR sgca OR sgct OR subependymoma OR teratoma*)	**219**

Table 6. ProQuest Dissertations & Theses Global search string.

ID	Search	**Hits**
S5	S3 AND S4	**5**
S4	title((anaplastic-oligodendroglioma* OR astrocytoma OR atrt OR atypical-teratoid-rhabdoid-tumor* OR atypical-teratoid-rhabdoid-tumour* OR brain-cancer* OR brain-neoplasm* OR brain-tumor* OR brain-tumour* OR chondroma* OR chordoma* OR choroid-plexus-carcinoma* OR choroid-plexus-papilloma* OR choroid-plexus-tumors OR craniopharyngioma* OR diffuse-intrinsic-pontine OR dipg OR dnt OR ependymoblastoma* OR ependymoma OR ependymoma* OR ganglioglioma OR gbm OR gct OR germ-cell-tumor* OR germ-cell-tumour* OR germinoma* OR glioblastoma* OR glioma OR gliomatosis-cerebri OR gliosarcoma OR hamartoma* OR hemangioblastoma* OR lipoma* OR medulloblastoma* OR meningioma* OR neurocytoma* OR neurofibroma* OR neuroma* OR oligodendroglioma OR pineal-cyst* OR pineal-tumor* OR pineal-tumour* OR pineoblastoma* OR pineoblastoma* OR pineocytoma* OR pituitary-adenoma* OR pituitary-carcinoma* OR pituitary-tumor* OR pituitary-tumour* OR pnet OR tumor-of-the-brain OR primitive-neuroectodermal-tumor* OR primitive-neuroectodermal-tumour* OR rathke's-cleft-cyst* OR sarcomas OR schwannoma* OR sega OR sgca OR sgct OR subependymoma OR teratoma*)) OR abstract((anaplastic-oligodendroglioma* OR astrocytoma OR atrt OR atypical-teratoid-rhabdoid-tumor* OR atypical-teratoid-rhabdoid-tumour* OR brain-cancer* OR brain-neoplasm* OR brain-tumor* OR brain-tumour* OR chondroma* OR chordoma* OR choroid-plexus-carcinoma* OR choroid-plexus-papilloma* OR choroid-plexus-tumors OR craniopharyngioma* OR diffuse-intrinsic-pontine OR dipg OR dnt OR ependymoblastoma* OR ependymoma OR ependymoma* OR ganglioglioma OR gbm OR gct OR germ-cell-tumor* OR germ-cell-tumour* OR germinoma* OR glioblastoma* OR glioma OR gliomatosis-cerebri OR gliosarcoma OR hamartoma* OR hemangioblastoma* OR lipoma* OR medulloblastoma* OR meningioma* OR neurocytoma* OR neurofibroma* OR neuroma* OR oligodendroglioma OR pineal-cyst* OR pineal-tumor* OR pineal-tumour* OR pineoblastoma* OR pineoblastoma* OR pineocytoma* OR pituitary-adenoma* OR pituitary-carcinoma* OR pituitary-tumor* OR pituitary-tumour* OR pnet OR tumor-of-the-brain OR primitive-neuroectodermal-tumor* OR primitive-neuroectodermal-tumour* OR rathke's-cleft-cyst* OR sarcomas OR schwannoma* OR sega OR sgca OR sgct OR subependymoma OR teratoma*))	11,124
S3	S1 OR S2	126
S2	title((oncolytic-adenovirus* OR oncolytic-adenoviral* OR icovir17 OR oads)) OR abstract((oncolytic-adenovirus* OR oncolytic-adenoviral* OR icovir17 OR oads))	104
S1	title((oncolytic-viral* OR oncolytic-virotherap* OR oncolytic-virus-therap* OR oncolytic-virus* OR oncorine OR ovt OR rigvir OR t-vec) AND (adenovirus* OR adenoviridae OR adenoviral*)) OR abstract((oncolytic-viral* OR oncolytic-virotherap* OR oncolytic-virus-therap* OR oncolytic-virus* OR oncorine OR ovt OR rigvir OR t-vec) AND (adenovirus* OR adenoviridae OR adenoviral*))	54

Table 7. Summary of search results before and after de-duplication.

Database searched	**Date searched**	**Results**
PubMed MEDLINE	02/28/2023	348
Cochrane Central Register of Controlled Trials	02/28/2023	6
Embase (Elsevier)	02/28/2023	550
CINAHL	02/28/2023	18
Scopus	02/28/2023	219
ProQuest Dissertation and Thesis Index	02/28/2023	5
Total		1187
After de-duplication		**695**