Journée scientifique SNOB
Société de
Neuro-Oncologie Bretonne

Actualités en Neuro-Oncologie

Docteur Elodie VAULEON

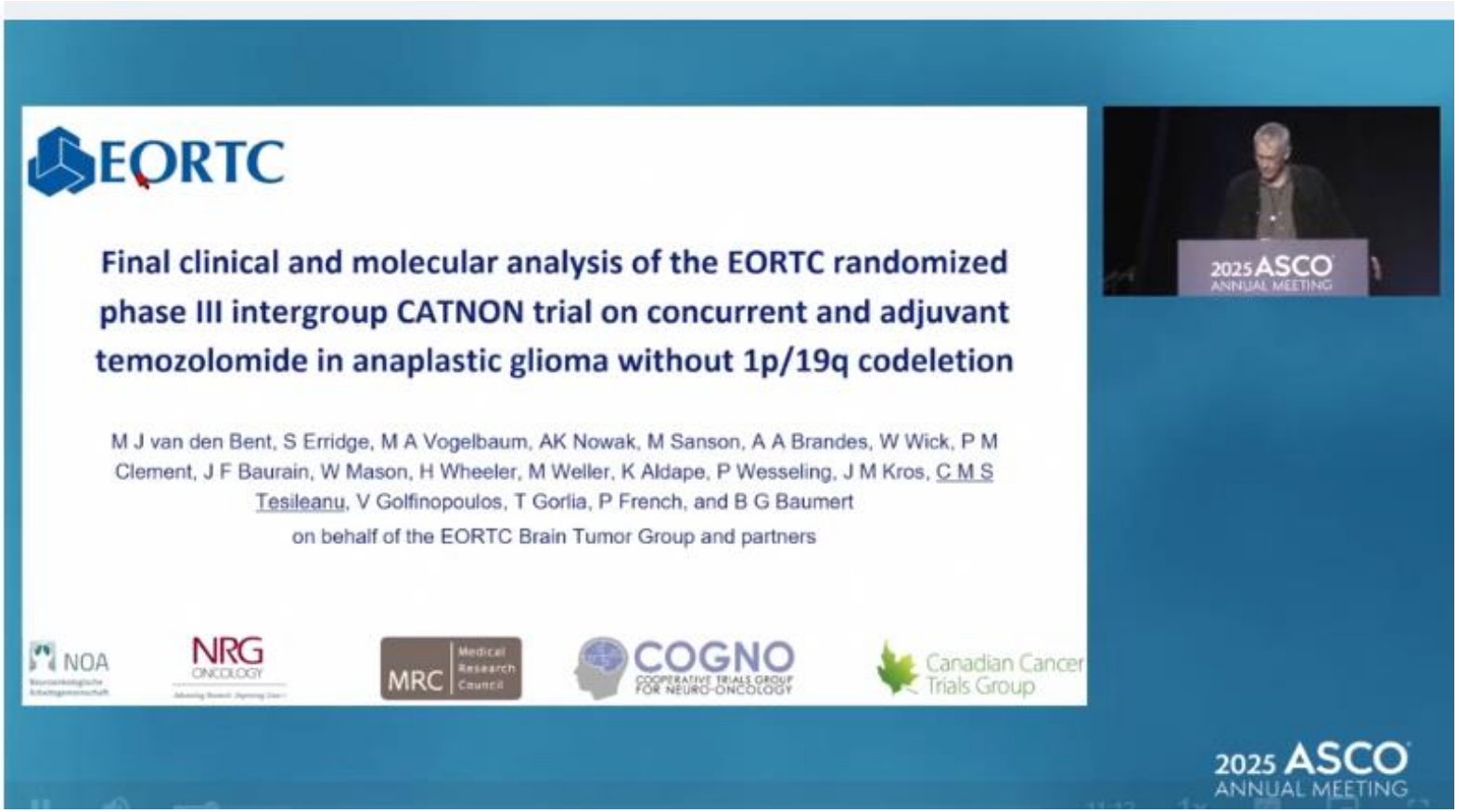
Vannes, le 10/10/2025

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliomes de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

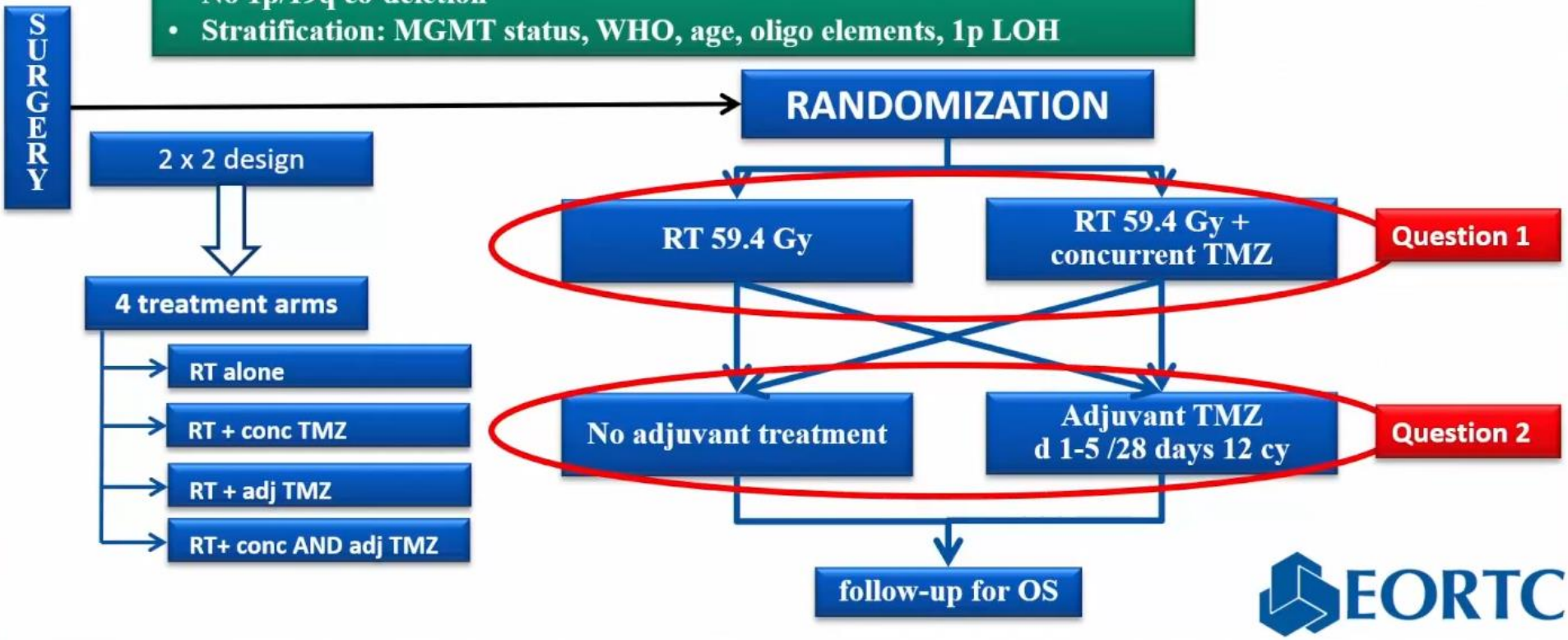
Actualités en Neuro-Oncologie

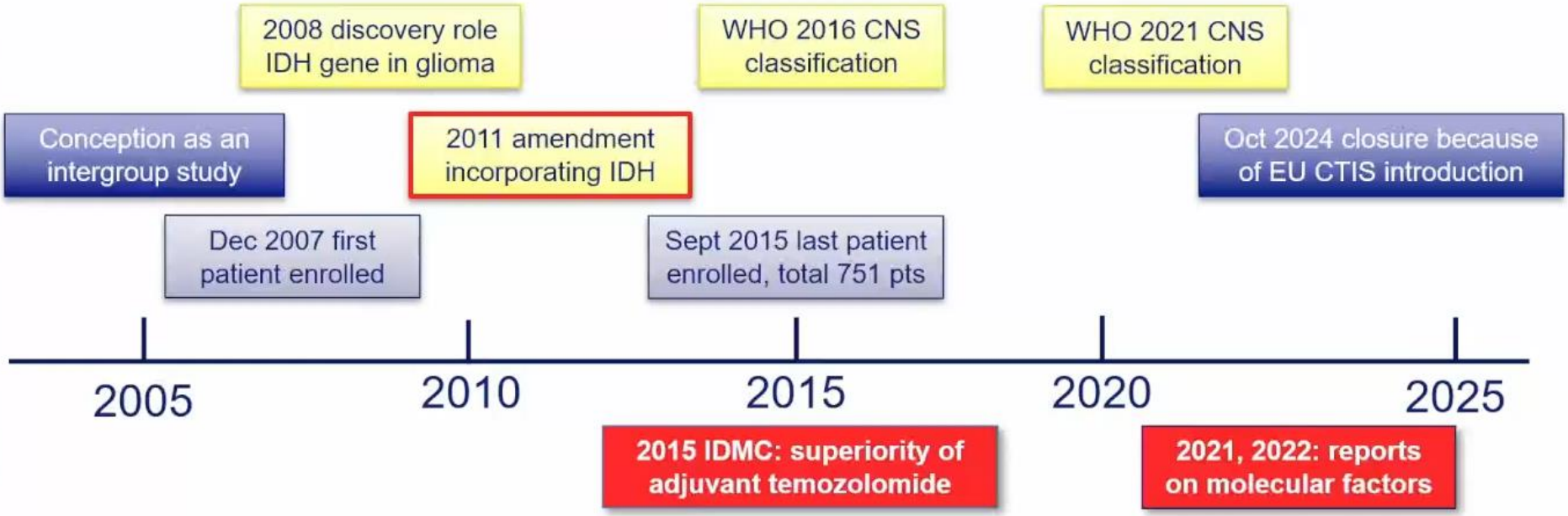
- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE


EORTC
Final clinical and molecular analysis of the EORTC randomized phase III intergroup CATNON trial on concurrent and adjuvant temozolomide in anaplastic glioma without 1p/19q codeletion
M J van den Bent, S Erridge, M A Vogelbaum, AK Nowak, M Sanson, A A Brandes, W Wick, P M Clement, J F Baurain, W Mason, H Wheeler, M Weller, K Aldape, P Wesseling, J M Kros, C M S Tesileanu, V Golfinopoulos, T Gorlia, P French, and B G Baumert
on behalf of the EORTC Brain Tumor Group and partners
NOA
NRG ONCOLOGY
MRC Medical Research Council
COGNO COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY
Canadian Cancer Trials Group
2025 ASCO ANNUAL MEETING
2025 ASCO ANNUAL MEETING

Objectives CATNON trial: does concurrent temozolomide and/or adjuvant temozolomide improve outcome in patients with anaplastic astrocytoma?

- Centrally confirmed grade III glioma
- No 1p/19q co-deletion
- Stratification: MGMT status, WHO, age, oligo elements, 1p LOH





Timelines CATNON trial

van den Bent et al, Lancet 2017;390:1645-53; Van den Bent et al, Lancet Oncology 2021;22:813-23; Tesileanu et al, Neuro-Oncol 2021;23:1547-59; Tesileanu et al, Clin Canc Res 2022;28:2527-35

Follow-up and events in May 2019 and October 2024

	n	2019 & 2021 Lancet Oncology report			2024 / ASCO 2025		
		Death	Progressed	Median follow-up	Death	Progressed	Median follow-up
All patients	751	367 (49%)	484 (64%)	**5.5 yrs**	499 (66%)	573 (76%)	**10.9 yrs**
With IDH wt glioma	216	32 (15%)			21 (10%)	205 (95%)	
With IDHmt glioma	444	152 (**34%**)	237 (**53%**)		245 (**55%**)	299 (**67%**)	

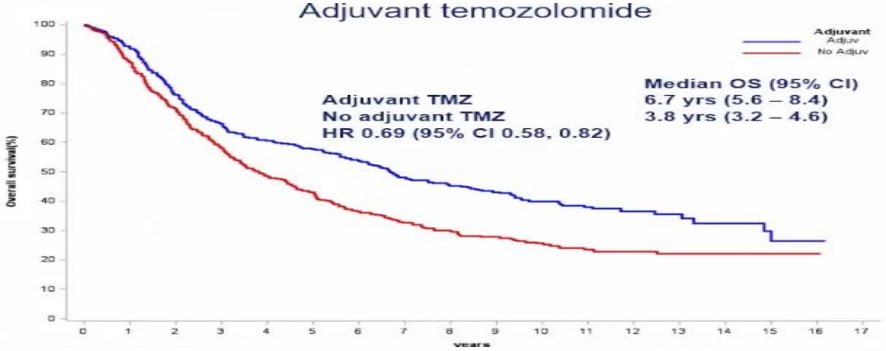
October 2024:
Subgroup of patients with IDHmt glioma: 199 (45%) of patients still alive

Centre Eugène Marquis

CATNON Overall Survival in the entire study population

Temozolomide arm
No temozolomide arm

Adjuvant temozolomide

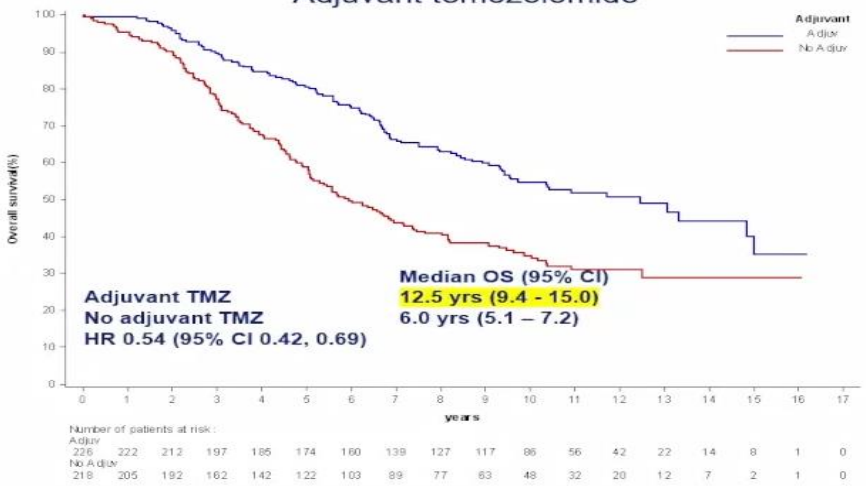


Concurrent temozolomide

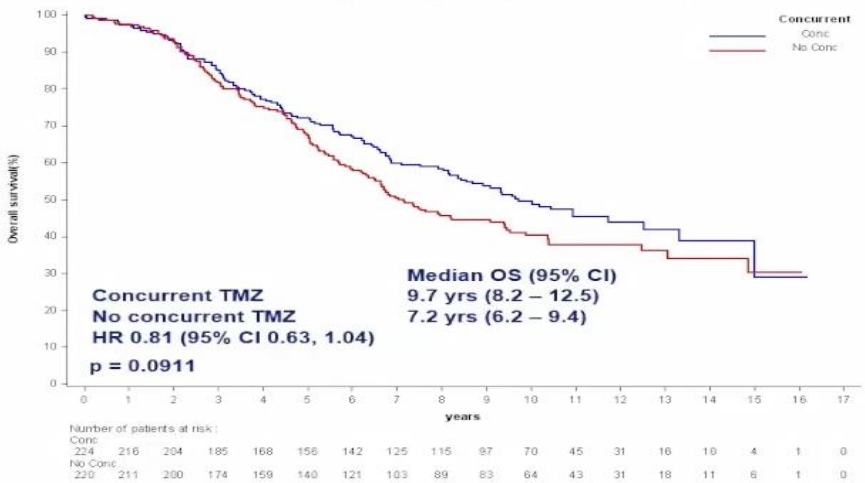
CATNON Overall Survival in the patients with IDHmt glioma

Temozolomide arm
No temozolomide arm

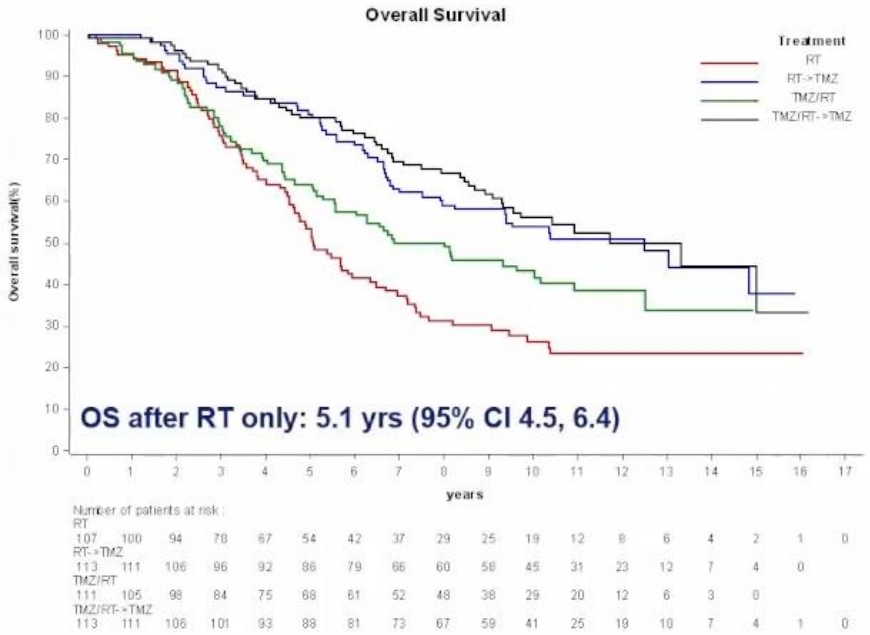
Adjuvant temozolomide



Concurrent temozolomide

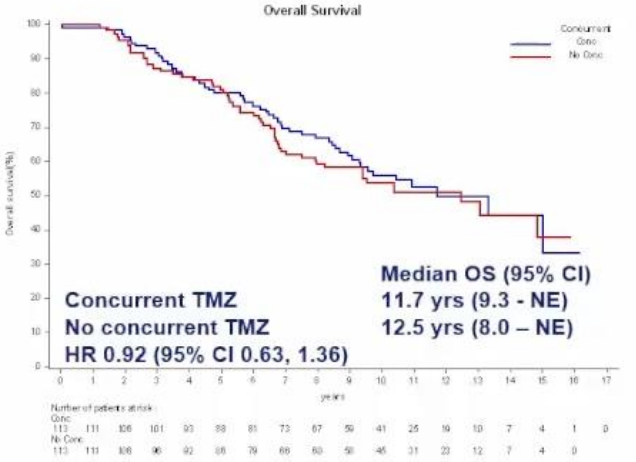


CATNON, exploratory analyses: OS in IDHmt glioma in all 4 study arms



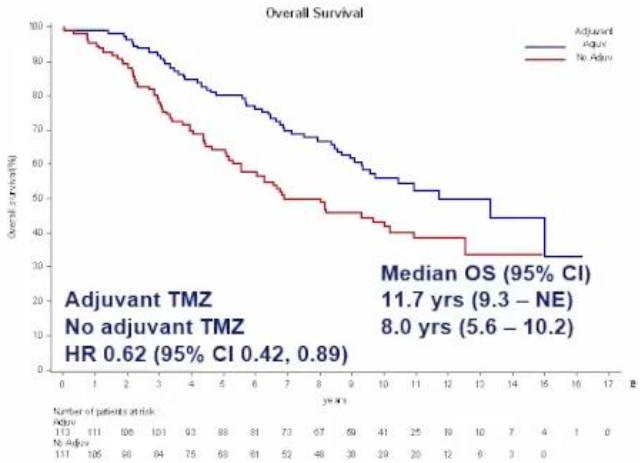
OS after RT only: 5.1 yrs (95% CI 4.5, 6.4)

Patients that received adjuvant temozolomide



Median OS (95% CI)
Concurrent TMZ 11.7 yrs (9.3 - NE)
No concurrent TMZ 12.5 yrs (8.0 – NE)
HR 0.92 (95% CI 0.63, 1.36)

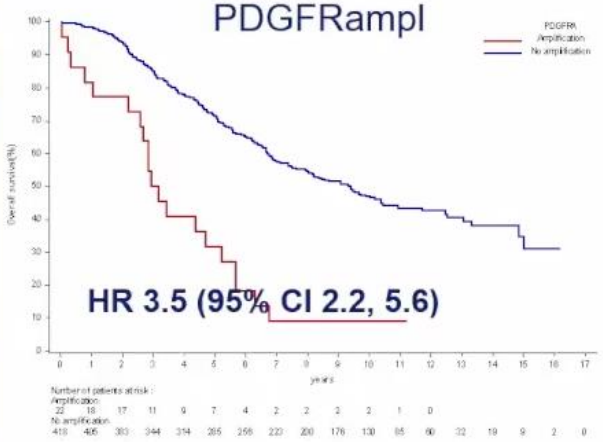
Patients that received concurrent temozolomide



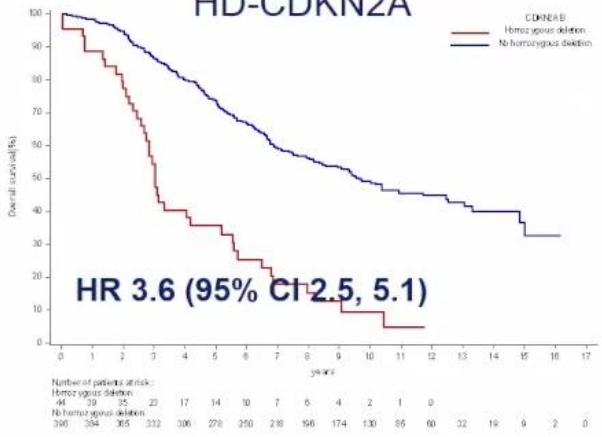
Median OS (95% CI)
Adjuvant TMZ 11.7 yrs (9.3 – NE)
No adjuvant TMZ 8.0 yrs (5.6 – 10.2)
HR 0.62 (95% CI 0.42, 0.89)

OS in patients with IDH mt in relation to molecular status

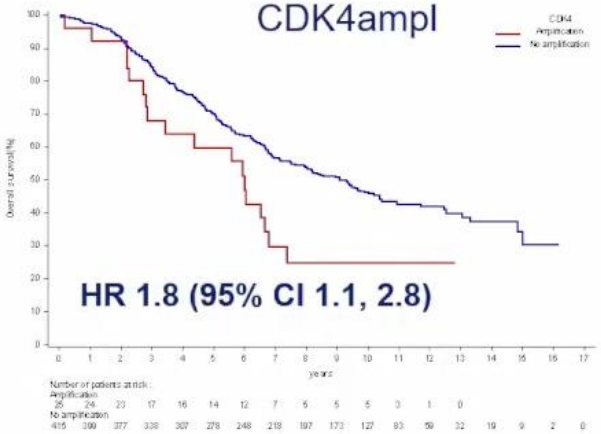
PDGFRampl



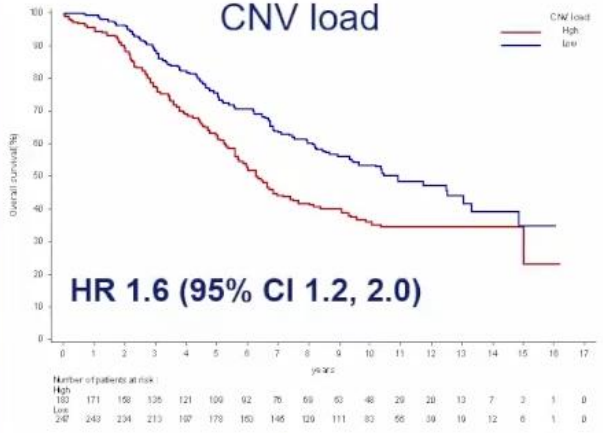
HD-CDKN2A



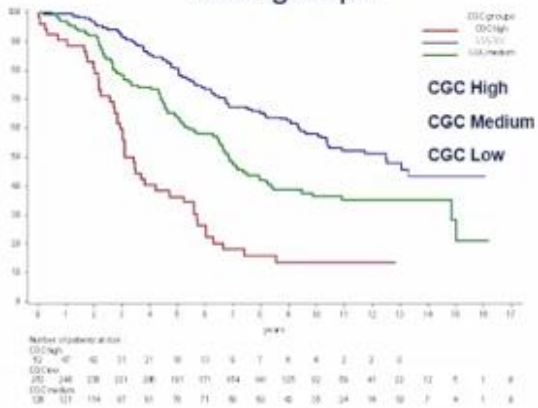
CDK4ampl



CNV load

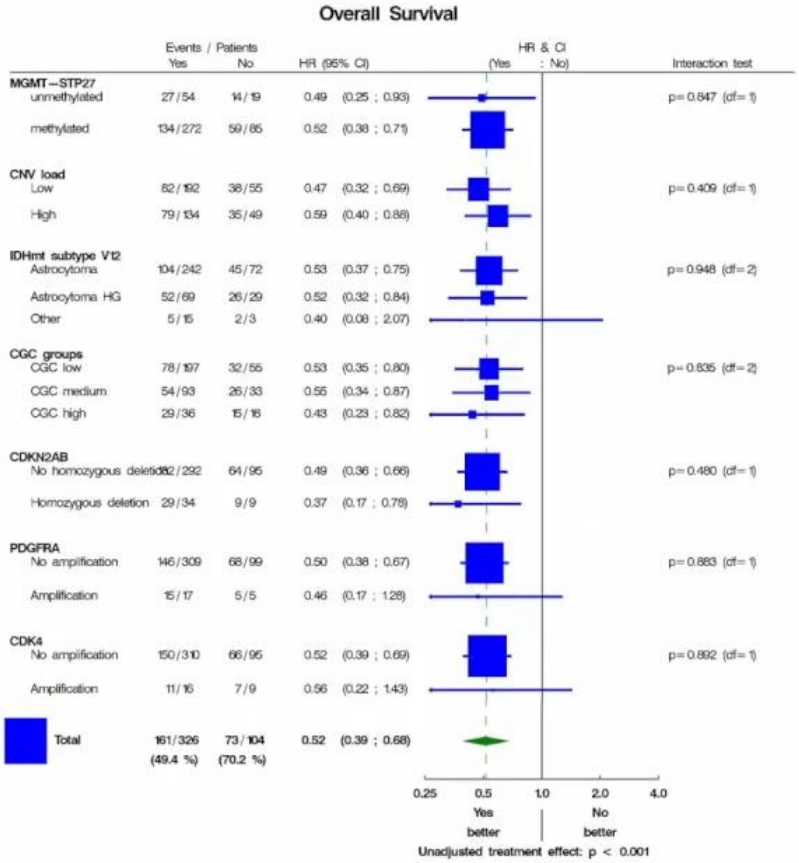


CGC groups



	Median (95% CI)	HR (95% CI)
CGC High	3.3 (2.8-4.7)	REF
CGC Medium	6.9 (5.6-8.2)	0.42 (0.29-0.62)
CGC Low	12.5 (10.2-NE)	0.24 (0.17-0.35)

Molecular prognostic markers in IDHmt astrocytoma grade 3 and outcome to RT + any temozolomide vs RT only



Forest plot:

None of the molecular markers associated with poor overall survival was predictive of (lack of) benefit to temozolomide

Conclusions final analyses CATNON trial in the IDHmt glioma patient subgroup

With median follow-up of 10.9 years and 45% of patients still alive

- Improved OS after 12 cycles of adjuvant temozolomide
  - Median OS after adjuvant TMZ ±12 years
- No benefit of concurrent temozolomide if adjuvant temozolomide is given
- ➢ Standard of care in more agressive IDHmt astrocytoma: radiotherapy followed by 12 cycles of adjuvant temozolomide
- None of the highly *prognostic* molecular markers *predictive* for outcome to temozolomide

EORTC

2025 ASCO ANNUAL MEETING

A Phase 2 Study of Pemigatinib for Pretreated Glioblastoma or Other Gliomas With Activating FGFR1-3 Alterations: Results From FIGHT-209

Enrico Franceschi,[1] Martin J. van den Bent,[2] Marc Sanson,[3] Andrew B. Lassman,[4] Giuseppe Lombardi,[5] Maria Vieito Villar,[6] Roy E. Strowd,[7] Juan Manuel Sepulveda Sanchez,[8] Catherine McBain,[9] Mina Lobbous,[10] Rikke Hedegaard Dahlrot,[11] Estela Pineda,[12] Delphine Larrieu,[13] Alessia Pellerino,[14] Yoshitaka Narita,[15] Stephen Joseph Bagley,[16] Lalanthica Yogendran,[17] Natalia Oliveira,[18] Yufei Guo,[18] Luisa Veronese,[18] Louis Viviers,[18] Manmeet Singh Ahluwalia[19]

2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Enrico Franceschi, MD

ASCO KNOWLEDGE CONQUERS CANCER

2025 ASCO

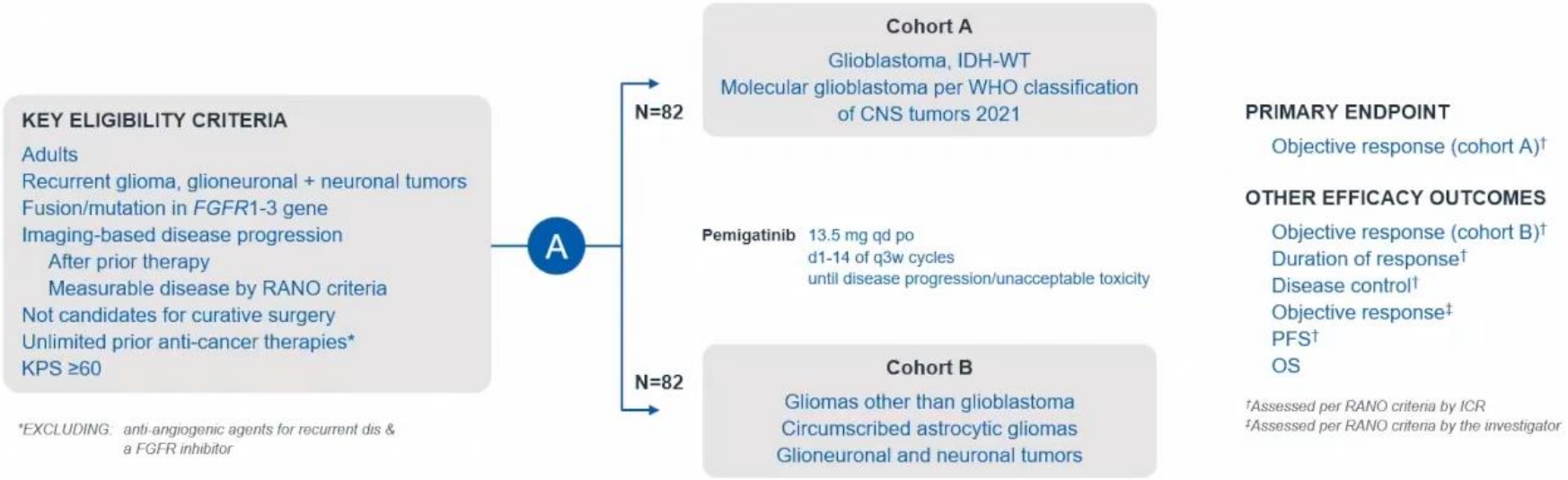
Centre Eugène Marquis RENNES

Background

- Recurrent gliomas, and in particular glioblastoma (GBM), represent a population with dismal prognosis and limited therapeutic options
  - In GBM, survival after first disease progression remains in the range of 6-8 months
- However, a small group of patients may benefit from targeted agents against specific molecular aberrations (eg, BRAF, NTRK)
- FGFR genomic alterations occur in ~8% of gliomas[1]
- FGFR1-3 alterations (fusions/rearrangements and mutations) have been successfully targeted in other cancer types (eg, cholangiocarcinoma)[1]
- Inhibition of FGFR1-3 with pemigatinib showed antitumor activity in a multi-histology basket trial (FIGHT-207)
  - Approximately 10% of participants had recurrent/progressive FGFR-altered GBM[2]
- We further investigated pemigatinib activity in primary brain tumors by performing an international, multicenter, single-arm, 2-cohort, phase 2 study specifically in adults with FGFR-altered pretreated gliomas
  - Conducted at 78 centers in 9 countries in North America, Europe, and Japan

unicancer

Study Design



CNS, central nervous system; FGFR, fibroblast growth factor receptor; ICR, independent central review; IDH-WT, isocitrate dehydrogenase-wildtype; OS, overall survival; PFS, progression-free survival; RANO, Response Assessment in Neuro-Oncology; WHO, World Health Organization.

Statistical Considerations

- One interim analysis (cohort A) and a final analysis were conducted

	Interim Analysis (Cohort A)	Final Analysis
Planned		
Timing	After 25 patients were RANO evaluable*	
Endpoints	Interim objective response	Objective response, DOR, DCR, PFS, OS
Futility	≤4 responses assessed by ICR	
Actual		
Data cutoff	August 16, 2023	December 17, 2024
Predefined target		Lower boundary of the 95% CI of ORR >15%

*≥2 post-baseline disease assessments per RANO by ICR or discontinued study treatment for reasons other than intolerable toxicity or discontinued from the study

CI, confidence interval; DCR, disease control rate; DOR, duration of response; ICR, independent central review; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RANO, Response Assessment in Neuro-Oncology.

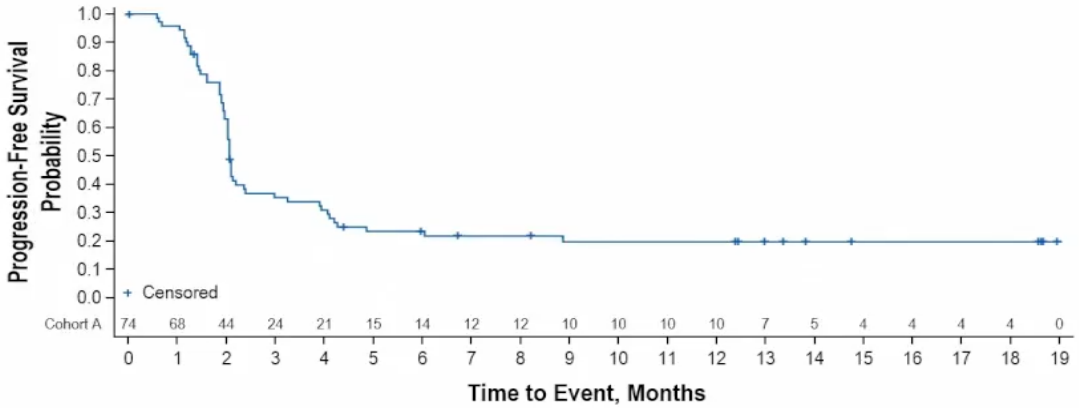
Patient Characteristics

Characteristic	Cohort A (n=74)	Cohort B (n=9)
Age, median (range), years	58 (20, 79)	32 (25, 60)
≥65 years, n (%)	19 (26)	0
Male, n (%)	44 (60)	6 (67)
Geographic region, n (%)		
Europe	54 (73)	6 (67)
North America	18 (24)	3 (33)
Asia Pacific (Japan)	2 (3)	0
Karnofsky Performance Status, n (%)		
90-100	35 (47)	3 (33)
70-80	34 (46)	5 (56)
60	5 (7)	1 (11)
***FGFR* alteration**, n (%)		
Fusion/rearrangement	65 (88)	1 (11)
Mutation	9 (12)	8 (89)
***FGFR* with alteration**, n (%)		
FGFR1	8 (11)	8 (33)
FGFR2	1 (1)	0
FGFR3	65 (88)	1 (11)

- Diagnosis (cohort B): circumscribed astrocytic tumor (n=5), glioneuronal tumor (n=3), and adult-type diffuse glioma (n=1)
- Most patients in cohort A had a *FGFR* fusion: 54 (73%) had FGFR3-TACC3
- Most patients in cohort B had a *FGFR1* mutation: K656E (n=6) and N546K (n=2)

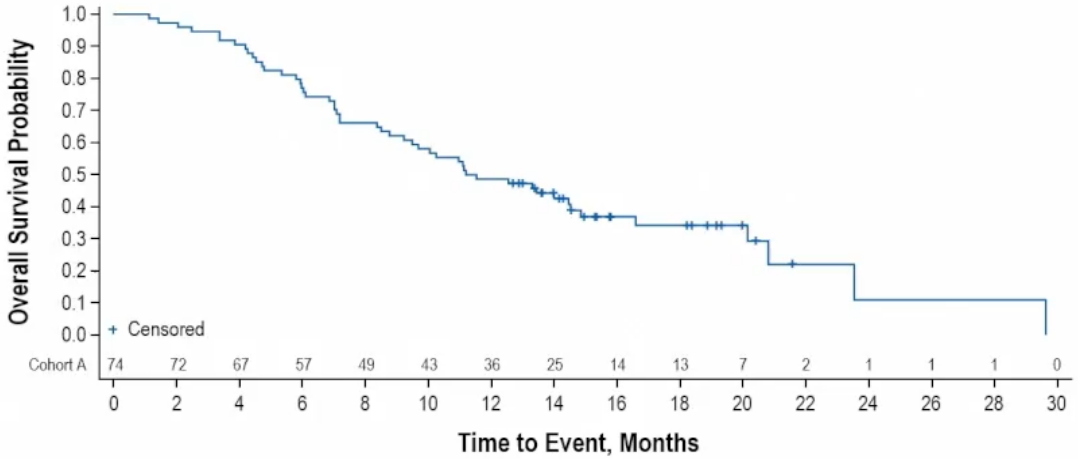
Characteristic	Cohort A (n=74)	Cohort B (n=9)
Prior surgical resection, n (%)	66 (89.2)	8 (88.9)
Completed standard radiotherapy, n (%)	72 (97)	4 (44)
With temozolomide	67 (91)	4 (44)
Systemic treatment at recurrence, n (%)		
Temozolomide	12 (16)	1 (11)
Nitrosourea with/without procarbazine and vincristine	8 (11)	1 (11)
Other chemotherapy	3 (41)	2 (22)
Immune checkpoint inhibitor	1 (1)	0
Bevacizumab	1 (1)	0
Other	4 (5)	0
Number of recurrences		
Pemigatinib at first recurrence	42 (57)	7 (78)
Pemigatinib after ≥2 recurrences	32 (43)	2 (22)

Efficacy (Cohort A) Assessed by ICR



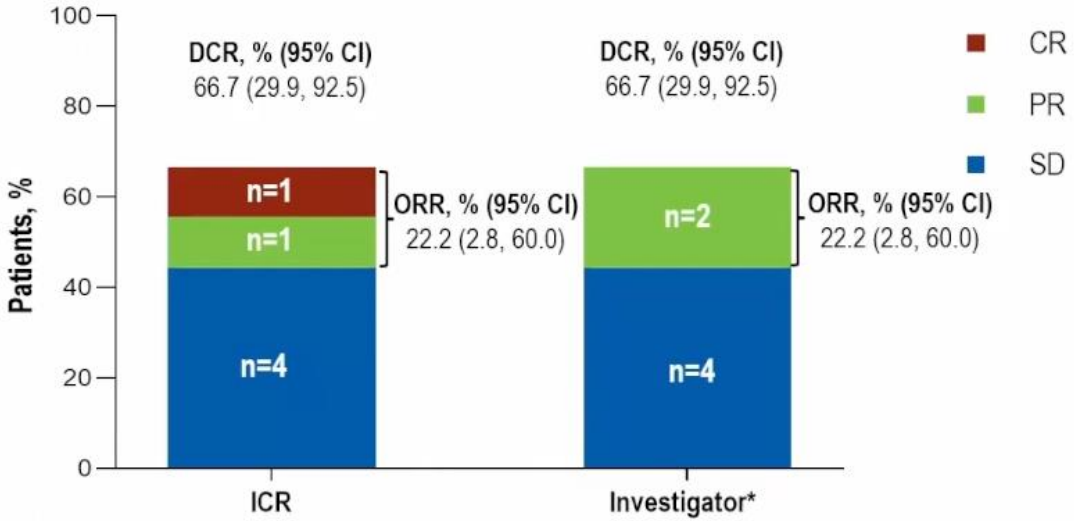
Efficacy Measure	n=74
PFS*	
Events, n (%)	55 (74.3)
Median (95% CI), months	2.1 (2.0, 2.4)
6-month rate, % (95% CI)	23.5 (14.3, 34.1)
12-month rate,% (95% CI)	19.8 (11.2, 30.3)

Efficacy (Cohort A)



Efficacy Measure	n=74
OS	
Events, n (%)	50 (67.6)
Median (95% CI), months	11.4 (9.2, 14.9)
12-month rate, % (95% CI)	48.6 (36.9, 59.4)

Efficacy (Cohort B) Assessed by ICR and Investigators



Efficacy measure	n=9
DOR†	
Median (95% CI), months	NR (NE, NE)
Estimated DOR of 6 months, % (95% CI)	100 (100, 100)
PFS‡	
Events, n (%)	4 (44.4)
Median (95% CI), months	NR (1.7, NE)
6-month rate, % (95% CI)	66.7 (28.2, 87.8)
OS	
Events, n (%)	2 (22.2)
Median (95% CI), months	24.1 (18.8, NE)
12-month rate, % (95% CI)	100 (100, 100)

- Median (range) follow-up was 22.1 (13.0, 25.9) months

CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; ICR, independent central review; NE, not evaluable; NR, not reached; PFS, progression-free survival; PR, partial response; SD, stable disease.

*Response unconfirmed. †Assessed by ICR; response confirmed. ‡Assessed by ICR.

Pemigatinib Safety Profile in Recurrent Gliomas

n (%)	Total (N=83)
Any TEAE	82 (99)
Treatment-related	79 (95)
Grade ≥3	30 (36)
Serious TEAE	17 (21)
Fatal TEAE	1 (1)
Modification to planned administration	
TEAEs leading to discontinuation	2 (2)*
TEAEs leading to dose interruption†	26 (31)
TEAEs leading to dose reduction‡	7 (8)

- Most TEAEs were of low-grade severity; only 2 patients discontinued owing to TEAEs

	Total (N=83)	
TEAE,§ n (%)	Any Grade	Grade ≥3
Hyperphosphatemia	67 (81)	0
Diarrhea	41 (49)	0
Fatigue	24 (29)	0
Alopecia	23 (28)	0
Hypophosphatemia	22 (27)	0
Constipation	20 (24)	1 (1)
Dry skin	16 (19)	0
Nail disorder	16 (19)	1 (1)
Headache	15 (18)	1 (1)
ALT Increased	14 (17)	0
Stomatitis	14 (17)	1 (1)
Asthenia	13 (16)	2 (2)
Dry mouth	13 (16)	0
Seizure	13 (16)	3 (4)

*Fatigue and herpes zoster (each n=1). †Most common TEAEs leading to dose interruption were hyperphosphatemia (n=3), asthenia, lipase increased, hypercalcemia, seizure, and confusional state (each n=2). ‡Most common TEAEs leading to dose reduction were hyperphosphatemia and onychomadesis (each n=2). §Occurring in ≥15% of patients in the safety population. AE, adverse event; ALT, alanine amino transferase; TEAE, treatment-emergent adverse event.

Conclusions

In cohort A (recurrent GBM)

- ORR did not reach the preplanned threshold of 28%
  - But ~50% patients had ≥2 relapses
  - Responses were observed in 8% of patients (including 6 partial responses) as assessed by investigator
- 6-month PFS rate was 23.5% in a heavily pretreated population
- Median OS and 12-month OS rates were encouraging (11.4 months and 48.6%, respectively)
- 16% of patients were able to receive pemigatinib for ≥12 months

In cohort B (non-GBM)

- Results were also encouraging for a biologic effect of this drug
- Of 9 patients, 1 had a complete response,1 had a partial response, and 4 had stable disease as assessed by ICR

- Adverse reactions in recurrent gliomas were consistent with known safety profile of pemigatinib

AcSé PEMIGATINIB ouvert à Brest et au CEM

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliomes de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- **GLIOBLASTOME et Gliomes de haut grade**
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Meta-Analysis > Neurosurg Rev. 2025 Sep 1;48(1):628. doi: 10.1007/s10143-025-03787-5.

Awake versus asleep craniotomy for eloquent glioblastoma: a systematic review and meta-analysis

Susan I Honeyman [1], Alexandros Boukas [2], Melika Akhbari [2], Blessing Okoli [2], Richard Stacey [2], Vasileios Apostolopoulos [2], Puneet Plaha [2 3]

Affiliations + expand

PMID: 40887547 DOI: 10.1007/s10143-025-03787-5

Abstract

Awake craniotomy (AC) can aid in preserving neurological function through intraoperative mapping of sensorimotor and language functions. It has been associated with increased extent of resection (EOR) and reduced neurological deficits in glioma patients. Most studies focused on low grade tumours and there remains limited evidence assessing utility of AC for glioblastoma (GB). This systematic review evaluates current evidence for safety and efficacy of GB resection under AC versus general anaesthetic (GA) conditions. We carried out a systematic review and meta-analysis of original studies assessing comparative outcomes of supratentorial GB resection via AC versus GA. Studies included patients > 18 years of age, with histopathological diagnosis of Grade 4 GB affecting an eloquent location. Medline, Embase and Pubmed were searched from inception to the 30th of June 2025. The outcomes assessed included: EOR, rates of temporary and permanent post-operative neurological deficits, survival, and functional outcomes. Eleven studies were included, with 1355 patients (402 AC and 953 GA resections). AC achieved greater percentage EOR (MD = 7.55 [CI 2.94-12.15], p = 0.001), and non-significant increase in rates of gross total resection (OR = 1.66 [CI 0.64-4.35], p = 0.30). The risk of developing a post-operative neurological deficit was significantly lower with AC (OR = 0.55 [CI:0.36-0.85], p = 0.008). Overall survival (HR = 7.99 [CI 2.29-13.69], p = 0.007) was significantly increased with AC but there was no significant difference in progression-free survival (HR = 2.03 [CI -1.32-5.37], p = 0.23). AC for eloquently located GB is associated with improved EOR, survival and lower risk of neurological complications. When feasible, AC should be considered for eloquent GB resection.

Meta-Analysis > J Neurooncol. 2025 Sep;174(2):271-301. doi: 10.1007/s11060-025-05058-1. Epub 2025 May 2.

Current trends in reoperation for recurrent glioblastoma: a meta-analysis (2007-2023)

Pavel S Pichardo-Rojas [1], Fabricio Garcia-Torrico [2], César B Espinosa-Cantú [3], Francisco A Rodriguez-Elvir [4], Andrea C Beltran-De la Fuente [5], Myriam S Hernandez-Garcia [6], James S Trippett [1], Alexis Morell [7], Ashish H Shah [8], Ricardo J Komotar [9], Yoshua Esquenazi [10] [11]

Affiliations + expand

PMID: 40314867 DOI: 10.1007/s11060-025-05058-1

Abstract

Purpose: Despite conflicting evidence, reoperation for recurrent glioblastoma (rGBM) achieving complete resection of enhancing-tumor (CRET) may offer benefits over partial resection or salvage therapy alone. However, pooled analyses remain limited.

Methods: A systematic search identified rGBM studies comparing reoperation and non-reoperation, including chemotherapy with/without radiotherapy, radiation-based therapies (RBT), and best supportive care (BSC).

Results: Thirty-six studies, comprising 10,738 patients, were included, with 2,806 undergoing reoperation. Nine propensity-score-matched studies and one clinical trial were identified. Mean overall survival (OS) favored reoperation (19.66 months) over chemotherapy with/without radiotherapy (12.56 months, $p < 0.00001$) and BSC (4.04 months, $p < 0.00001$), but not over chemotherapy alone (14.60 months) or RBT (14.26 months)($p > 0.05$). Multivariate OS favored reoperation over chemotherapy with/without radiation(HR = 0.62,95%CI:0.50-0.76,$p < 0.00001$), but not to stereotactic radiosurgery (SRS) (HR = 0.52,95%CI:0.25-1.08,$p = 0.08$) or chemotherapy alone (HR = 0.80,95%CI:0.63-1.00,$p = 0.05$). Progression-free survival after recurrence (PFS2) was only compared between reoperation and chemotherapy with/without radiotherapy, favoring reoperation (8.36 vs. 4.97 months, $p < 0.00001$). Multivariate analysis also favored reoperation (HR = 0.56, 95% CI:0.41-0.76,$p = 0.0002$).The mean post-recurrence survival (PRS) was 12.18 months in the reoperation group, 9.19 months in the chemotherapy with/without radiotherapy, and 9.64 months in SRS. Multivariate PRS favored reoperation over chemotherapy with/without radiotherapy (HR = 0.78, 95%CI: 0.62-0.98,$p = 0.04$). CRET with < 1 cm^3 residual tumor correlated with improved PRS over incomplete resection (HR: 0.54, 95%CI:0.39-0.73, $p = 0.04$).

Conclusion: The role of reoperation in rGBM remains uncertain. While it may improve survival in selected cases, limited high-quality data hinder definitive conclusions. Achieving CRET may correlate with improved PRS over partial resection. Further prospective trials are necessary to guide optimal management of rGBM.

J Neurooncol. 2025 May;173(1):49-57. doi: 10.1007/s11060-025-04946-w. Epub 2025 Mar 31.

Long-term survival, patterns of progression, and patterns of use for patients with newly diagnosed glioblastoma treated with or without Tumor Treating Fields (TTFields) in a real-world setting

Devon C Riegel [1], Britta L Bureau [2], Patrick Conlon [3], Gordon Chavez [3], Jennifer M Connelly [2]

Affiliations + expand

PMID: 40163248 PMCID: PMC12040967 DOI: 10.1007/s11060-025-04946-w

Abstract

Purpose: Tumor Treating Fields therapy (TTFields) is an FDA-approved locoregional treatment for patients with newly diagnosed glioblastoma (ndGBM). Previous trial data showed the addition of TTFields to standard TMZ-based therapy to significantly improve overall survival (OS), but real-world data is lacking, particularly with long follow-up duration. Here, we report real-world survival, patterns of progression, and patterns of use for patients for patients with ndGBM treated with or without TTFields.

Methods: Patients diagnosed with GBM and treated with standard of care therapy at the Medical College of Wisconsin between March 2015-March 2023 were included. Survival outcomes were assessed and compared across groups who received or did not receive TTFields therapy during maintenance treatment. Patients were followed through March 1, 2024.

Results: A total of 208 patients (TTFields: n = 109; No-TTFields: n = 99) were included for analysis. Baseline characteristics were consistent across groups. Median OS and PFS were significantly improved for the TTFields group vs. No-TTFields group (median OS: 21.7 vs. 17.7 months, p = 0.029; median PFS: 12.4 vs. 9.6 months, p = 0.047). Patients treated with TTFields exhibited a higher rate of non-local progression vs. No-TTFields group. Median OS and PFS were each significantly longer for the ≥ 75% usage group compared with < 75% via matched analysis.

Conclusion: The results of this study reveal an association between TTFields use and long-term survival benefit, consistent with pivotal trial findings. TTFields use is associated with a higher incidence of non-local patterns of progression, and TTFields device usage ≥ 75% is associated with increased progression-free and long-term survival.

J Cancer Res Clin Oncol. 2025 Jun 2;151(6):179. doi: 10.1007/s00432-025-06171-4.

Limited survival benefit in patients diagnosed with glioblastoma post–2016: a SEER population based registry analysis

Shaurya Dhingra [1], Matthew Koshy [1], Mark Korpics [2]

Affiliations + expand

PMID: 40455099 PMCID: PMC12130152 DOI: 10.1007/s00432-025-06171-4

Abstract

Background: The EF14 clinical trial reported an improvement in median overall survival (OS) from 16.0 months to 20.9 months in patients with glioblastoma (GBM) who received treatment with tumor treating fields (TTFs). This study evaluates overall survival in a large population-based cohort of patients with GBM before and after FDA approval of TTFs in 2015.

Methods: A total of 27,534 patients from the Surveillance, Epidemiology and End Results (SEER) database with GBM who underwent surgery and post-operative radiotherapy were grouped into three diagnosis periods: those diagnosed pre-temozolomide (2000-2004), those diagnosed post-temozolomide (2005-2015), and those diagnosed post-TTFs (2016-2020). Overall survival (OS) was calculated using the Kaplan-Meier method, and multivariate Cox regression models were employed to estimate hazard ratios (HR).

Results: GBM diagnosis in the post-TTFs period was associated with a median OS of 15 months (95% CI 14-15 months) compared to a median OS of 14 months (95% CI 14-14 months, $p < 0.001$) for GBM diagnosis in the post-temozolomide/pre-TTFs period. 24-months OS was 25.6% (95% CI 24.5-26.8%) in the post-TTFs period and 24.7% (95% CI 24.0-25.4%) in the post-temozolomide/pre-TTFs period. In a multivariate model accounting for clinical characteristics, diagnosis in the post-TTFs period as compared to the post-temozolomide/pre-TTFs period was significantly associated with OS (HR: 0.941, 95% CI 0.912-0.972, $p < 0.001$).

Conclusion: This population-based cohort demonstrated minimal change in survival for patients diagnosed with GBM before and after FDA approval of TTFs in 2015.

Clinical Trial > Med. 2025 Sep 12;6(9):100708. doi: 10.1016/j.medj.2025.100708. Epub 2025 Jun 4.

Efficacy and safety of adjuvant TTFields plus pembrolizumab and temozolomide in newly diagnosed glioblastoma: A phase 2 study

Dongjiang Chen [1], Son B Le [1], Ashley P Ghiaseddin [2], Harshit Manektalia [1], Ming Li [3], Adam O'Dell [1], Maryam Rahman [4], David D Tran [5]

Affiliations + expand

PMID: 40466642 DOI: 10.1016/j.medj.2025.100708

Abstract

Background: Immune checkpoint inhibitors (ICIs) have shown limited success in glioblastoma due to the tumor's profoundly immunosuppressive microenvironment. Tumor treating fields (TTFields), a non-invasive electric field therapy, activate the type I interferon (T1IFN) pathway via DNA sensor-dependent inflammasomes, promoting in situ immunization against glioblastoma.

Methods: In this phase 2 study (this study was registered at ClinicalTrials.gov: NCT03405792), 31 newly diagnosed glioblastoma patients were enrolled post-chemoradiation to evaluate synergy between TTFields, pembrolizumab, and temozolomide. The primary endpoint was progression-free survival (PFS) compared to case-matched controls treated with TTFields and temozolomide alone. Secondary endpoints included overall survival (OS), response rate, safety, and immune correlates assessed through single-cell transcriptomics and T cell clonotyping of blood and tumor samples.

Findings: Among 26 patients treated per protocol, the median PFS was 12.0 vs. 5.8 months in controls (HR 0.377, 95% CI 0.217-0.653; p = 0.0026), and the median OS was 24.8 vs. 14.6 months (HR 0.522, 95% CI 0.301-0.905; p = 0.0477). Patients undergoing biopsy had longer PFS (27.2 vs. 9.6 months; HR 0.37, 95% CI 0.16-0.85; p = 0.014) and OS (31.6 vs. 18.8 months; HR 0.4, 95% CI 0.17-0.92; p = 0.023) compared to maximal resection. Severe adverse events constituted 7.5% of treatment-related toxicities. TTFields promoted clonal T cell expansion via a T1IFN-driven trajectory, while pembrolizumab supported adaptive replacement of these clones, sustaining T cell activation and memory formation, especially in biopsy-only patients.

Conclusions: These findings demonstrate synergy between TTFields and ICIs, particularly in patients with high tumor burden, and support further study in larger trials.

> Neurooncol Pract. 2025 Jan 17;12(2):291-300. doi: 10.1093/nop/npaf006. eCollection 2025 Apr.

Temozolomide chemotherapy for patients with newly diagnosed glioblastoma in the CENTRIC EORTC 26071–22072 and CORE trials: Does time of administration matter?

Marjolein Geurts [1] [2], Luzia Berchtold [3] [4], Franz Koenig [3], Burt Nabors [5], David A Reardon [6], Joerg C Tonn [7] [8], Roger Stupp [9], Thierry Gorlia [10], Michael Weller [11], Matthias Preusser [12]; EORTC Brain Tumor Group

Affiliations + expand

PMID: 40110070 PMCID: PMC11913640 DOI: 10.1093/nop/npaf006

Abstract

Background: Preclinical work and retrospective studies suggest that temozolomide chemotherapy in glioblastoma may be more effective when administered in the morning rather than the evening. Here we examine the effect of timing in a large cohort of patients in 2 contemporaneous randomized clinical trials.

Methods: We assessed toxicity and survival data in patients with newly diagnosed glioblastoma enrolled in the CENTRIC EORTC 26071-22072 (n = 545, MGMT methylated) and CORE (n = 265, MGMT unmethylated) trials. We compared the outcome and toxicity of patients who took maintenance (adjuvant) temozolomide (TMZ) either in the morning (TMZ-m), afternoon (TMZ-a) or in the evening (TMZ-e).

Results: In CENTRIC and CORE, n = 102/260 (39%) and 50/198 (25%) received TMZ in the morning versus n = 35/260 (13%) and 34/198 (17%) in the evening. There was no difference in overall survival (OS) between the TMZ-m and TMZ-e groups (CENTRIC: adjusted mOS 20.6 months (95% confidence interval [CI], 18.4-23.4) TMZ-m vs 21.1 months (95% CI, 18.4-24.5) TMZ-e; adjusted hazard ratio (HR), 0.93 (95% CI, 0.63-1.39); P = .7; CORE: adjusted mOS, 10.9 months (95%CI, 9.7-11.8) TMZ-m vs 11.4 months (95%CI, 9.9-12.9) TMZ-e; adjusted HR, 0.87, 95%CI, 0.55-1.38); P = .6). The TMZ-m group had a higher proportion of bone marrow toxicity (CENTRIC: TMZ-m 33% vs TMZ-e 11%, P = .013, CORE: TMZ-m 24% vs TMZ-e 3%, P < .01).

Conclusion: In this post hoc analysis, we found no difference in outcome based on the time of TMZ administration. Bone marrow toxicity might occur more frequently when temozolomide is administered in the morning. Given the limitation to data from deceased patients only, these analyses should be viewed as exploratory only.

> Radiother Oncol. 2025 Aug 10:211:111088. doi: 10.1016/j.radonc.2025.111088.
Online ahead of print.

Quality assurance in the randomized multicentre phase III trial EORTC–1709–BTG/CCTG CE.8 (MIRAGE) for glioblastoma: Results of the radiotherapy delineation benchmark case procedure

Jonas Willmann [1], Joost J C Verhoeff [2], Orit Kaidar-Person [3], André Abrunhosa-Branquinho [4], Enrico Clementel [5], Coreen Corning [5], Daniel Portik [6], Luiza Souza [5], Jaap C Reijneveld [7], Frederic Dhermain [8], Coen Hurkmans [9], Angelo Filippo Monti [10], Jordi Saez [11], Warren P Mason [12], Michael Weller [13], Patrick Roth [13], Nicolaus Andratschke [14]

Affiliations + expand

PMID: 40796015 DOI: 10.1016/j.radonc.2025.111088

Abstract

Purpose: The multicentre randomised phase III trial EORTC-1709-BTG/CCTG CE.8 (MIRAGE) (NCT03345095) analysed the addition of the proteasome inhibitor marizomib to temozolomide-based chemoradiotherapy with 60 Gy in 30 fractions in patients with newly diagnosed glioblastoma. Here, we analysed the benchmark case procedure for delineation and planning radiotherapy quality assurance (RTQA) that was performed before patient inclusion.

Materials and methods: Prior to trial activation, all participating centers were required to submit a benchmark case for radiotherapy volume delineation and planning. Submissions were prospectively reviewed by the RTQA team, and in cases of unacceptable variations, centers were required to revise and resubmit the same case until protocol compliance was achieved. Structure sets and dose distributions of the same benchmark patient submitted by participating centres were analysed. We determined the rate and causes of variations of glioblastoma target volumes (TV) and organs at risk (OAR) from the protocol-specified delineation guidelines. Delineation interobserver variability before and after RTQA review were quantified using the Dice similarity coefficient (DSC) with respect to ground truth contours at first and final submission of the benchmark case. The influence of reducing delineation interobserver variability on dose parameters of ground truth structures was determined.

Results: The delineations by 88 institutes were judged by RTQA reviewers to contain "unacceptable" variations in 80 % (n = 70) of the cases. TV contours were more frequently deemed unacceptable than organs at risk (72 % vs 55 %). After RTQA review, the mean DSC significantly improved for TV (GTV: 0.77 vs 0.82, p = 0.002; CTV: 0.85 vs 0.88, p < 0.0001; PTV: 0.85 vs 0.88, p < 0.0001), brainstem (0.87 vs 0.88, p = 0.007), cochlea (0.58 vs 0.62, p = 0.004) and optic nerve (0.65 vs 0.67, p = 0.0005), indicating reduced interobserver variability. The delineation adjustments after RTQA review resulted in a significant increase of the mean CTV $D_{98\%}$ (+2.2 Gy, +4%, p = 0.005), indicating an improved target coverage. Doses to organs at risk did not change significantly but still met predefined constraints.

Conclusions: Variations in the delineation of target volumes and organs at risk were frequently judged as "unacceptable" during the RTQA review process. Besides a significant increase of CTV coverage, the impact of variations on organ at risk dosimetry was minor, suggesting a potentially negligible effect on toxicity outcomes. Quantitative metrics to assess delineation variations should be explored to improve the RTQA process in clinical trials and routine practice, aiming to flag delineation variations that confer an effect on tumour control or toxicity.

Practice Guideline > Radiother Oncol. 2025 Jan:202:110594. doi: 10.1016/j.radonc.2024.110594. Epub 2024 Oct 24.

ESTRO–EANO guideline on target delineation and radiotherapy for IDH–mutant WHO CNS grade 2 and 3 diffuse glioma

Brigitta G Baumert [1], Jaap P M Jaspers [2], Vera C Keil [3], Norbert Galldiks [4], Ewa Izycka-Swieszewska [5], Beate Timmermann [6], Anca L Grosu [7], Giuseppe Minniti [8], Umberto Ricardi [9], Frédéric Dhermain [10], Damien C Weber [11], Martin van den Bent [12], Roberta Rudà [13], Maximilian Niyazi [14], Sara Erridge [15]

Affiliations + expand

PMID: 39454886 DOI: 10.1016/j.radonc.2024.110594

Free article

Abstract

Purpose: This guideline will discuss radiotherapeutic management of IDH-mutant grade 2 and grade 3 diffuse glioma, using the latest 2021 WHO (5th) classification of brain tumours focusing on: imaging modalities, tumour volume delineation, irradiation dose and fractionation.

Methods: The ESTRO Guidelines Committee, CNS subgroup, nominated 15 European experts who identified questions for this guideline. Four working groups were established addressing specific questions concerning imaging, target volume delineation, radiation techniques and fractionation. A literature search was performed, and available literature was discussed. A modified two-step Delphi process was used with majority voting resulted in a decision or highlighting areas of uncertainty.

Results: Key issues identified and discussed included imaging needed to define target definition, target delineation and the size of margins, and technical aspects of treatment including different planning techniques such as proton therapy.

Conclusions: The GTV should include any residual tumour volume after surgery, as well as the resection cavity. Enhancing lesions on T1 imaging should be included if they are indicative of residual tumour. In grade 2 tumours, T2/FLAIR abnormalities should be included in the GTV. In grade 3 tumours, T2/FLAIR abnormalities should also be included, except areas that are considered to be oedema which should be omitted from the GTV. A GTV to CTV expansion of 10 mm is recommended in grade 2 tumours and 15 mm in grade 3 tumours. A treatment dose of 50.4 Gy in 28 fractions is recommended in grade 2 tumours and 59.4 Gy in 33 fractions in grade 3 tumours. Radiation techniques with IMRT are the preferred approach.

Practice Guideline > Pract Radiat Oncol. 2025 Sep-Oct;15(5):451-471.
doi: 10.1016/j.prro.2025.05.014. Epub 2025 Jun 25.

Radiation Therapy for WHO Grade 4 Adult-Type Diffuse Glioma: An ASTRO Clinical Practice Guideline

Debra Nana Yeboa [1], Steve E Braunstein [2], Alvin Cabrera [3], Kevin Crago [4], Evanthia Galanis [5], Eyas M Hattab [6], Dwight E Heron [7], Jiayi Huang [8], Michelle M Kim [9], John P Kirkpatrick [10], Jonathan P S Knisely [11], Mary Frances McAleer [12], Shearwood McClelland 3rd [13], Michael T Milano [14], Jennifer Moliterno [15], Alyx Porter [16], Kristin J Redmond [17], Daniel M Trifiletti [18], Christina Tsien [19], Bhanu Prasad Venkatesulu [20], Yevgeniy Vinogradskiy [21], Lisa Bradfield [22], Amanda R Helms [22], Joseph A Bovi [23]

Affiliations + expand
PMID: 40578479 DOI: 10.1016/j.prro.2025.05.014

Abstract

Purpose: The central nervous system World Health Organization (WHO) grade 4 adult-type diffuse glioma represents one of the most aggressive and challenging primary brain tumors. This guideline aims to provide evidence-based recommendations for the multidisciplinary management of these tumors, focusing on diagnosis, initial treatment, reirradiation, and health disparities, while acknowledging that present literature primarily represents historical histologic grade 4 glioblastoma.

Methods: The American Society for Radiation Oncology convened a task force to address 4 key questions focused on indications for radiation therapy (RT) and/or adjunctive therapies (eg, systemic therapy, alternating electric field therapy), appropriate regimens for external beam RT after initial biopsy/resection including variables such as pretreatment characteristics, target volumes, technique, dose, reirradiation indications and techniques, and health disparities. Recommendations are based on a systematic literature review and created using a predefined consensus-building methodology and system for grading evidence quality and recommendation strength.

Results: Following maximum safe resection, molecular and pathologic diagnosis, and prognostic stratification of WHO grade 4 adult-type diffuse glioma, concurrent RT with temozolomide followed by adjuvant temozolomide is recommended for eligible patients and incorporation of alternating electric field therapy is conditionally recommended. In elderly patients, hypofractionated RT with concurrent and adjuvant temozolomide is conditionally recommended. In frail patients, supportive and palliative care is conditionally recommended following multidisciplinary, patient-centered discussion. Appropriate reirradiation techniques, with or without additional systemic therapies, can be considered and are conditionally recommended in patients following pathologic or advanced imaging confirmation of WHO grade 4 diffuse glioma recurrence. Health disparities exist in patients with WHO grade 4 adult-type diffuse glioma and attention is necessary to improve outcomes and increase clinical trial enrollment for underserved populations.

Conclusions: These evidence-based recommendations and current practice adoption patterns inform best clinical practices on the management of WHO grade 4 adult-type diffuse glioma. Future advancements in personalized medicine, biomarker discovery, and novel therapies are essential to improving outcomes. The integration of multidisciplinary care and participation in future clinical trials, especially in underserved populations, is crucial in addressing the poor outcomes among WHO grade 4 adult-type diffuse glioma.

Randomized Controlled Trial > Int J Radiat Oncol Biol Phys. 2025 Apr 1;121(5):1168-1181.
doi: 10.1016/j.ijrobp.2024.11.094. Epub 2024 Nov 28.

Toxicity and Efficacy of Different Target Volume Delineations of Radiation Therapy Based on the Updated Radiation Therapy Oncology Group/National Research Group and European Organization for Research and Treatment of Cancer Guidelines in Patients With Grade 3-4 Glioma: A Randomized Controlled Clinical Trial

Yanfang Qiu [1], Yanxian Li [1], Cuihong Jiang [1], Xiangwei Wu [1], Wen Liu [1], Changgen Fan [1], Xu Ye [1], Lili He [1], Shuai Xiao [1], Qi Zhao [1], Wenqiong Wu [1], Kailin Chen [1], Chao Tan [1], Yuyi Li [1], Hui Wang [2], Feng Liu [3]

Affiliations + expand

PMID: 39615657 DOI: 10.1016/j.ijrobp.2024.11.094

Abstract

Purpose: Our study aimed to evaluate the safety and efficacy of radiation therapy (RT) in the treatment of grade 3-4 glioma by comparing the updated Radiation Therapy Oncology Group (RTOG)/National Research Group (NRG) with European Organization for Research and Treatment of Cancer (EORTC) guidelines for target volume delineation.

Methods and materials: A total of 245 patients with newly diagnosed World Health Organization grade 3-4 glioma were enrolled and randomly assigned (1:1 ratio) to undergo postoperative RT with concurrent and maintenance temozolomide. The radiation target volume delineation was determined by using either the updated RTOG/NRG (n = 122) or EORTC guidelines (n = 123). The primary endpoint was the toxicity associated with treatment. Progression-free survival (PFS) and overall survival (OS) were considered secondary endpoints.

Results: No differences in low- or high-grade toxicities between the 2 groups, and neither group exhibited grade 5 toxicities. No significant differences in neurologic toxicities were observed between the RTOG/NRG and EORTC groups. The median PFS in the RTOG/NRG group and the EORTC group was 11.0 months (95% confidence interval [CI], 7.1-14.9 months) and 10.0 months (95% CI, 3.8-16.2 months), respectively (P = .73). The median OS in the RTOG/NRG group and the EORTC group was 19.5 months (95% CI, 14.2-24.8 months) and 18.5 months (95% CI, 12.8-24.2 months), respectively (P = .80). In patients with isocitrate dehydrogenase wild-type glioblastoma, there were no significant differences between the RTOG/NRG group and the EORTC group in median PFS (8.0 months [95% CI, 6.8-9.2 months] vs. 8.0 months [95% CI, 7.0-9.0 months], P = .38) and median OS (12.0 months [95% CI, 7.2-16.8 months] vs. 11.0 months [95% CI, 9.7-12.3 months], P = .10).

Conclusions: Compared with EORTC principles, postoperative RT according to RTOG/NRG principles did not increase treatment-related toxicities and was equally effective for patients with grade 3-4 glioma, including the subgroup of patients with isocitrate dehydrogenase wild-type glioblastoma.

> Neuro Oncol. 2025 Aug 13:noaf177. doi: 10.1093/neuonc/noaf177. Online ahead of print.

Glioblastoma in Adults: A Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) Consensus Review on Current Management and Future Directions

Patrick Y Wen [1], Michael Weller [2], Eudocia Q Lee [1], Mehdi Touat [3], Mustafa Khasraw [4], Rifaquat Rahman [5], Michael Platten [6], Michael Lim [7], Frank Winkler [8], Craig Horbinski [9], Roel G W Verhaak [10], Raymond Y Huang [11], Manmeet S Ahluwalia [12], Nathalie L Albert [13], Joerg-Christian Tonn [14], David Schiff [15], Jill S Barnholtz-Sloan [16], Quinn Ostrom [17], Kenneth D Aldape [18], Tracy T Batchelor [19], Ranjit S Bindra [20], E Antonio Chiocca [21], Timothy F Cloughesy [22], John F DeGroot [23], Pim French [24], Evanthia Galanis [25], Norbert Galldiks [26], Mark R Gilbert [27], Monika E Hegi [28], Andrew B Lassman [29], Emilie Le Rhun [30], Minesh P Mehta [31], Ingo K Mellinghoff [32], Giuseppe Minniti [33], Patrick Roth [2], Marc Sanson [34], Martin J B Taphoorn [35], Andreas von Deimling [36], Tobias Weiss [2], Wolfgang Wick [37], Gelareh Zadeh [38], David A Reardon [1], Susan M Chang [39], Susan C Short [40], Martin J van den Bent [24], Matthias Preusser [41]

Affiliations + expand

PMID: 40827022 DOI: 10.1093/neuonc/noaf177

Abstract

Glioblastoma is the most common type of malignant primary brain tumor and a major cause of morbidity and mortality. In 2021 the World Health Organization updated the classification of Central Nervous System (CNS) tumors to restrict glioblastomas to isocitrate dehydrogenase-wildtype (IDHwt) tumors, improving understanding of the prognosis and optimal therapy for these tumors. This revision also enables more homogeneous populations of patients to be enrolled into clinical trials, facilitating the evaluation of novel therapies. In this updated consensus review from the Society for Neuro-Oncology (SNO) and the European Association of Neuro-Oncology (EANO), the current management of patients with glioblastoma is discussed. In addition, novel therapies such as immunotherapies, viral therapies, targeted molecular therapies, theranostics and antibody-drug conjugates will be reviewed, as well as the current challenges and future directions for research.

Nat Med. 2025 Sep 5. doi: 10.1038/s41591-025-03928-9. Online ahead of print.

Molecularly matched targeted therapies plus radiotherapy in glioblastoma: the phase 1/2a N²M² umbrella trial

Wolfgang Wick [1], Lisa-Marie Lanz [2], Antje Wick [3], Inga Harting [4], Susan Dettmer [2], Abigail K Suwala [5], Ralf Ketter [6], Ghazaleh Tabatabai [7 8], Corinna Seliger [3 9], Martin Glas [10], Michael C Burger [11], Marco Timmer [12], Florian A Ringel [13 14], Iris Mildenberger [15 16], Walter J Schulz-Schaeffer [17], Frank Winkler [3], Laila König [18], Christel Herold-Mende [19], Andreas Eisenmenger [2], Stefan M Pfister [20], Mirjam Renovanz [7 8 21], Martin Bendszus [4], Felix Sahm [22], Michael Platten [15 16], Tobias Kessler [3]

Affiliations + expand

PMID: 40913172 DOI: 10.1038/s41591-025-03928-9

Abstract

Advances in molecular understanding and diagnostic precision of glioblastoma enable the identification of key genetic alterations in a timely manner and, in principle, allow treatments with targeted compounds based on molecular markers. Here we report the results of the phase 1/2 umbrella trial NCT Neuro Master Match (N²M²), which evaluated targeted treatments in 228 patients with newly diagnosed glioblastoma without O6-methylguanine DNA-methyltransferase promoter hypermethylation. Stratification for treatment was conducted by a trial-specific molecular tumor board across five subtrials, each evaluating a targeted therapy-alectinib, idasanutlin, palbociclib, vismodegib or temsirolimus-selected according to the best-matching molecular alteration. Patients without matching alterations were randomized between subtrials without strong biomarkers using atezolizumab and asunercept, and the standard of care (SOC), temozolomide. All received radiotherapy. The primary endpoints were dose-limiting toxicities (phase 1) and progression-free survival at 6 months (PFS-6; phase 2). Secondary endpoints included safety and tolerability, as well as overall survival (OS). The subtrials for alectinib and vismodegib did not open as they did not have matching patients. The idasanutlin subtrial (n = 9) was terminated early at the discretion of the manufacturing company. The temsirolimus subtrial (n = 46) demonstrated a PFS-6 of 39.1% and median OS of 15.4 months in patients with activated mammalian target of rapamycin (mTOR) signaling compared to a PFS-6 at 18.5% in the SOC group (n = 54), meeting the primary endpoint. The atezolizumab (n = 42), asunercept (n = 26) and palbociclib (n = 41) subtrials did not meet the primary endpoint for efficacy. The safety signals of N²M² match prior experiences with the drugs in quality and quantity; no relevant negative interaction with the parallel radiotherapy was noted. The results of the N²M² trial support further investigation of temsirolimus in addition to radiotherapy in patients with newly diagnosed glioblastoma with activated mTOR signaling. ClinicalTrials.gov registration: NCT03158389 .

Neurooncol Adv. 2025 May 26;7(1):vdaf032. doi: 10.1093/noajnl/vdaf032. eCollection 2025 Jan-Dec.

Ipilimumab with temozolomide vs. temozolomide alone after surgery and chemoradiotherapy in recently diagnosed glioblastoma: a randomized phase II clinical trial

Nicholas F Brown [1], Catherine McBain [2], Lucy Brazil [3], Sharon Peoples [4], Sarah Jefferies [5], Fiona Harris [5], Anup Vinayan [6], Puneet Plaha [7], Claire Brooks [8], Samia Hussain [9], Susan J Dutton [9], Jonathan Cook [9], Stasya M Ng [8], Stephanie Levy [8], Timothy Coutts [8], Paul Mulholland [10] [1]

Affiliations + expand

PMID: 40800123 PMCID: PMC12342986 DOI: 10.1093/noajnl/vdaf032

Abstract

Background: Glioblastoma confers a bleak prognosis, with median survival of less than a year. This trial evaluated whether addition of the CTLA-4 immune checkpoint inhibitor ipilimumab to standard therapy improves survival in patients with recently diagnosed glioblastoma.

Methods: Ipi-Glio was a stratified randomized, open-label, multicenter, academic phase II study. Patients with recently diagnosed de novo glioblastoma following completion of chemoradiotherapy were randomized 2:1 to ipilimumab + temozolomide (Arm A) vs temozolomide alone (Arm B), stratified to extent of surgery and MGMT promotor methylation. Primary endpoint was overall survival. Secondary endpoints included progression-free survival at 18 months, overall survival at 3 years, and toxicity (≥Grade 3).

Results: One hundred nineteen patients were randomized (79 to Arm A, 40 to Arm B). Patient characteristics (Arm A vs B): median age 57 vs 49 years; male sex 70 vs 65%, gross total resection 61 vs 60%, tumor MGMT promotor methylation 39 vs 40%. Median overall survival was 18 months (60% CI 16.0, 23.9) in Arm A vs 23.0 months (17.3, 26.4) in Arm B (adjusted HR 1.09, 60% CI 0.86,1.38, one-sided $P = .62$; logrank $P = .75$). Progression-Free Survival: 10.8 vs 12.5 months (Arm A vs B) (adjusted HR 1.34, 1.06-1.68, one-sided $P = .86$;logrank $P = .42$). Grade 3 or above adverse events: 53% Arm A vs 43% Arm B ($P = .27$).

Conclusions: No benefit was observed with the addition of ipilimumab to temozolomide in patients with recently diagnosed glioblastoma following chemoradiotherapy. This study does not support further investigation of this regimen in this setting.

Clinical Trial > Neuro Oncol. 2025 May 15;27(4):1092-1101. doi: 10.1093/neuonc/noae247.

Phase 2 trial of veliparib, local irradiation, and temozolomide in patients with newly diagnosed high-grade glioma: a Children's Oncology Group study

Matthias A Karajannis [1], Arzu Onar-Thomas [2], Tong Lin [2], Patricia A Baxter [3], Daniel R Boué [4], Bonnie L Cole [5], Christine Fuller [6], Sofia Haque [7], Nada Jabado [8], John T Lucas Jr [9], Shannon M MacDonald [10], Celeste Matsushima [11], Namrata Patel [12], Christopher R Pierson [4], Mark M Souweidane [13] [14], Diana L Thomas [4], Michael F Walsh [1], Wafik Zaky [15], Sarah E S Leary [16], Amar Gajjar [17], Maryam Fouladi [18], Kenneth J Cohen [19]

Affiliations + expand

PMID: 39560182 PMCID: PMC12083075 (available on 2025-11-19) DOI: 10.1093/neuonc/noae247

Abstract

Background: The outcome for pediatric patients with high-grade glioma (HGG) remains poor. Veliparib, a potent oral poly(adenosine diphosphate-ribose) polymerase (PARP) 1/2 inhibitor, enhances the activity of radiotherapy and DNA-damaging chemotherapy.

Methods: We conducted a single-arm, non-randomized phase 2 clinical trial to determine whether treatment with veliparib and radiotherapy, followed by veliparib and temozolomide, improves progression-free survival in pediatric patients with newly diagnosed HGG without H3 K27M or BRAF mutations, compared to patient-level data from historical cohorts with closely matching clinical and molecular features. Following surgical resection, newly diagnosed children with non-metastatic HGG were screened by rapid central pathology review and molecular testing. Eligible patients were enrolled on Stratum 1 (IDH wild-type) or Stratum 2 (IDH mutant).

Results: Both strata were closed to accrual for futility after planned interim analyses. Among the 23 eligible patients who enrolled on Stratum 1 and received protocol therapy, the 1-year event-free survival (EFS) was 23% (standard error, SE = 9%) and the 1-year overall survival (OS) was 64% (SE = 10%). Among the 14 eligible patients who enrolled on Stratum 2 and received protocol therapy, the 1-year EFS was 57% (SE = 13%) and 1-year OS was 93% (SE = 0.7%).

Conclusions: Rapid central pathology review and molecular testing for eligibility were feasible. The protocol therapy including radiation, veliparib, and temozolomide was well tolerated but failed to improve outcomes compared to clinically and molecularly matched historical control cohorts treated with higher doses of alkylator chemotherapy.

Clinical Trial > Int J Radiat Oncol Biol Phys. 2025 Jul 1;122(3):605-610.
doi: 10.1016/j.ijrobp.2025.02.020. Epub 2025 Mar 8.

A Phase 2 Study of Multiparametric Magnetic Resonance Imaging–Guided High–Dose Response–Adaptive Radiation Therapy With Concurrent Temozolomide in Patients With Newly Diagnosed Glioblastoma: Results From an Interim Analysis

Michelle M Kim [1], Madhava P Aryal [2], Krithika Suresh [3], Benjamin S Rosen [2], Hemant Parmar [4], Daekeun You [2], Denise Leung [5], Nathan Clarke [5], John Fortunato [5], Wajd Al-Holou [6], Jason Heth [6], David Altshuler [6], Todd Hollon [6], Donna M Edwards [2], Daniel R Wahl [7], Theodore S Lawrence [2], Yue Cao [8]

Affiliations + expand

PMID: 40058709 PMCID: PMC12146080 (available on 2026-07-01)
DOI: 10.1016/j.ijrobp.2025.02.020

Abstract

Purpose: Biologically-informed radiation therapy (RT) targeting an adversely prognostic hypercellular/hyperperfused imaging phenotype in patients with newly diagnosed glioblastoma (GBM) may improve outcomes by identifying emerging regions of treatment resistance associated with overall survival, and is under investigation in an ongoing phase 2 trial (NCT04574856) of individualized, response-adaptive RT.

Methods and materials: In this single-arm phase 2 study, patients with newly diagnosed GBM after resection undergo dose-intensified chemoradiation targeting the residual hypercellular (TV_{HCV}, 2 SD above mean intensity contralateral normal brain) and hyperperfused tumor volume (TV_{CBV}, 1 SD above contralateral normal frontal lobe gray matter) identified using high b-value diffusion-weighted and dynamic contrast-enhanced perfusion magnetic resonance imaging. The combination of TV_{HCV} and TV_{CBV} (TV_{HCV}/TV_{CBV}) is treated to 50 Gy in 20 fractions (2.5 Gy/fraction), and after mid-RT reassessment, the persistent and developing TV_{HCV}/TV_{CBV} is treated to 30 Gy in 10 fractions (3 Gy/fraction). The primary endpoint is improvement in overall survival, with planned interim safety analysis.

Results: At interim analysis, 16 of 30 patients were enrolled. Median age was 58 years (range, 29-75) and 69% were male. No patient underwent biopsy only, and 50% had gross total resection; 19% had O^6-methylguanine-DNA methyltransferase methylated tumors. Median TV_{HCV}/TV_{CBV} was 6.9 cc (range, 1.9-42.8) pre-RT and 30% (range, 1%-72%) was nonenhancing. By mid-RT, TV_{HCV}/TV_{CBV} was reduced to 4.2 cc (range, 0.8-34.3) and 47% (range, 3%-74%) was nonenhancing. The TV_{HCV}/TV_{CBV} persisting from pre-RT to mid-RT was 2.3 cc (range, 0-24.2), with an additional 1.8 cc (range, 0.3-20.6) newly developing outside of the initial region. All patients underwent adaptive replanning for boost without interruption. Planned interim analysis determined an acceptable rate of neurologic toxicity and safety to continue enrollment.

Conclusions: Individualized, response-adaptive chemoradiation using an advanced imaging biomarker to assess emerging and especially nonenhancing regions of treatment resistance in patients with GBM is feasible, with short-term safety and longer-term efficacy outcomes anticipated with completion of accrual.

> BMC Med Imaging. 2025 Sep 26;25(1):386. doi: 10.1186/s12880-025-01929-1.

Heterogeneity phenotypes in recurrent glioblastoma: a multimodal MRI–based spatial mapping framework for precision treatment

Yan Zhu [1], Dian Huang [2], Yang Ji [2], Ranchao Wang [3], Yang Li [3], Yuhao Xu [4], Yan Zhuang [5], Zhe Liu [6 7], Yuefeng Li [8], Wei Wang [9]

Affiliations + expand

PMID: 41013339 DOI: 10.1186/s12880-025-01929-1

Abstract

Background: To develop a multimodal magnetic resonance imaging (MRI)-based spatial mapping framework for quantitatively characterizing intratumoral heterogeneity in recurrent glioblastoma (rGBM), identifying distinct imaging subregions, and classifying heterogeneity phenotypes predictive of treatment response and survival outcomes.

Methods: A total of 140 rGBM patients were recruited and underwent standardized diffusion-weighted imaging (DWI) and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI). Pixel-wise colocalization of apparent diffusion coefficient (ADC) and DCE-MRI features identified four Multimodal Imaging Subregions (MIS). Entropy and Moran's I quantified heterogeneity, and hierarchical clustering defined imaging phenotypes. Treatment response to 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), bevacizumab (Bev) + stereotactic radiotherapy (SRT), and Bev + CCNU was assessed by volumetric and component-level changes. Survival analyses were performed using Kaplan-Meier and multivariate Cox models.

Results: MIS4, defined by low ADC and slow-rising enhancement, was consistently treatment-resistant. Three imaging phenotypes with distinct heterogeneity patterns demonstrated significant prognostic stratification across regimens. Phenotype A showed the best outcomes under Bev-based regimens, while Phenotype B responded better to CCNU. Imaging phenotypes independently predicted progression-free survival (PFS) and overall survival (OS).

Conclusion: This framework enables spatially resolved, phenotype-based analysis of rGBM heterogeneity using routine MRI. Imaging phenotypes serve as non-invasive biomarkers to guide personalized treatment planning and outcome prediction in recurrent glioblastoma.

Clinical Trial > Cancer. 2025 Aug 15;131(16):e70015. doi: 10.1002/cncr.70015.

Lenvatinib plus pembrolizumab for patients with previously treated select solid tumors: Results from the phase 2 LEAP-005 study recurrent glioblastoma cohort

Sun Young Rha [1], Eduardo Castanon [2], Sanjeev Gill [3], Helene Senellart [4], Juanita Lopez [5], Iván Márquez-Rodas [6], Iván Victoria [7], Tae Min Kim [8], Zamie Lwin [9], Michael C Burger [10], Matteo Simonelli [11,12], Philippe A Cassier [13], Andrew E Hendifar [14], Paolo A Ascierto [15], Corina Dutcus [16], Chinyere E Okpara [17], Razi Ghori [18], Fan Jin [18], Roman Groisberg [18], Luis Villanueva [19]

Affiliations + expand

PMID: 40808295 PMCID: PMC12351156 DOI: 10.1002/cncr.70015

Abstract

Background: Patients with recurrent glioblastoma (GBM) have a poor prognosis and limited treatment options. The authors report the efficacy and safety of lenvatinib plus pembrolizumab in participants with recurrent GBM enrolled in the phase 2, multicohort LEAP-005 study (NCT03797326).

Methods: Eligible participants had histologically confirmed GBM (World Health Organization grade IV) with disease progression since previous treatment, and one or more prior lines of therapy. Participants were enrolled regardless of tumor programmed cell death ligand 1 (PD-L1) status and received oral lenvatinib 20 mg per day plus intravenous pembrolizumab 200 mg every 3 weeks. The dual primary end points were objective response rate (ORR; per Response Assessment in Neuro-Oncology by blinded independent central review) and safety.

Results: A total of 101 participants were enrolled, with median (range) follow-up of 23.7 (16.4–46.6) months. The median (range) duration of treatment with lenvatinib plus pembrolizumab was 3.4 (0.3–32.2) months. The ORR (95% confidence interval [CI]) was 20% (13%–29%), with 20 participants achieving a partial response, and the median (range) duration of response was 3.7 (1.4+ to 27.6) months. Median (95% CI) progression-free survival was 3.0 (2.7–4.0) months and median (95% CI) overall survival was 8.6 (7.4–10.8) months. Responses were observed regardless of PD-L1 status. Treatment-related adverse events occurred in 93 participants (92%; grade 3–5, n = 41 [41%]). Two participants died due to treatment-related adverse events (intestinal perforation and pneumonitis).

Conclusions: The combination of lenvatinib plus pembrolizumab demonstrated antitumor activity in a small subpopulation of participants with recurrent GBM as second-line or later treatment. The safety profile was manageable.

> Neurooncol Pract. 2024 Sep 25;12(2):209-218. doi: 10.1093/nop/npae091. eCollection 2025 Apr.

Health-related quality of life in patients with progressive glioblastoma treated with combined bevacizumab and lomustine versus lomustine only: Secondary outcome of the randomized phase III EORTC 26101 study

Linda Dirven [1] [2], Abigirl Machingura [3], Martin J van den Bent [4], Corneel Coens [3], Andrew Bottomley [3], Alba A Brandes [5], Julien Domont [6], Ahmed Idbaih [7], Johan A F Koekkoek [1] [2], Jaap C Reijneveld [8], Michael Platten [9], Wolfgang Wick [10] [11], Martin J B Taphoorn [1] [2]

Affiliations + expand

PMID: 40110057 PMCID: PMC11913650 DOI: 10.1093/nop/npae091

Abstract

Background: Progression-free survival, but not overall survival, was prolonged with bevacizumab and lomustine compared to lomustine only in the randomized phase 3 European Organization for Research and Treatment of Cancer (EORTC) 26101 study.

Objective: To evaluate the impact of treatment on health-related quality of life (HRQoL) in progressive glioblastoma patients participating in the EORTC 26101 study.

Methods: Patients with progressive glioblastoma, after standard radio-chemotherapy, were 2:1 randomized to either BEV/LOM or LOM. HRQoL was a secondary trial outcome and assessed using the EORTC QLQ-C30 and QLQ-BN20 questionnaires at baseline, and subsequently every 12 weeks. Predefined scales for analysis were global health status (GH), physical functioning, social functioning (SF), motor dysfunction, and communication deficit. The primary endpoint was HRQoL during the last assessment up to week 36. Moreover, time to HRQoL deterioration (TTD) and HRQoL deterioration-free survival (DFS) were calculated.

Results: Out of 437 patients, 402 (92%) patients had a baseline HRQoL assessment, which dropped to 66% at week 36. During the last assessment up to week 36, no differences were observed for predefined scales, apart from SF being clinically relevant lower in the combination arm (mean 66.0 versus 81.0, $p = .001$). Of note, the baseline SF score was 66.4 for patients in the combination arm, showing stable SF. Median DFS was significantly longer in the combination arm (12.4 weeks) compared to lomustine alone (6.7 weeks), reflecting the difference in time to progression between arms. TTD, not including progression as an event, was not different between treatment arms (median 13.0 versus 12.9 weeks).

Conclusion: The addition of bevacizumab to lomustine did not negatively affect HRQoL during the progression-free period.

Clinical Trial > Sci Rep. 2025 Jul 1;15(1):21064. doi: 10.1038/s41598-025-06675-6.

A phase 1 safety and feasibility trial of a ketogenic diet plus standard of care for patients with recently diagnosed glioblastoma

L J Amaral [#1,2,3], Gillian Gresham [#1,4,2], Sungjin Kim [5], Mourad Tighiouart [5], Thomas A Nelson [6], Amelia Welborn [7], Laura Lockshon [8], Brandon Noorvash [1,9], Jeremy D Rudnick [1,10], Scott A Irwin [1,11,2,12], Stephen J Freedland [1,2,13,3], Jethro Hu [14,15,16,17]

Affiliations + expand

PMID: 40595067 PMCID: PMC12215994 DOI: 10.1038/s41598-025-06675-6

Abstract

Despite great interest, there is limited clinical evidence to support the use of a ketogenic diet (KD) for cancer patients. We conducted a single-arm phase 1 trial of a KD among patients with recently diagnosed glioblastoma (GBM) receiving standard-of-care (SOC) treatment. Adults with GBM within 3 months of diagnosis followed a supervised 16-week intervention of a 3:1 KD (Fat(g): Carbohydrate + Protein(g)) plus SOC chemoradiation. The primary outcome was safety, evaluated by weekly assessments of weight and body mass index (BMI). Secondary outcomes included feasibility (pre-specified as > 50% of patients maintaining blood ketone levels > 0.3 mM over 50% of study days), progression-free survival (PFS), overall survival (OS), health-related quality-of-life, and cognitive function. Twice daily blood glucose and ketones, weight/BMI, physical activity, and sleep were assessed by remote monitoring. Seventeen patients were evaluable: 53% women, median age 55, median Karnofsky Performance Status 85. All subjects met the primary safety objective with no instances of excessive weight loss or related serious adverse events. Adherence was high: all 17 patients maintained nutritional ketosis (≥ 0.3 mM/dL) > 50% of study days. Median PFS and OS were 12.9 months and 29.4 months from KD initiation respectively. Quality of Life, symptom control, and cognitive function remained stable or improved, although these did not reach statistical significance. This phase 1 trial demonstrates that KD is safe and feasible for GBM patients receiving SOC, may improve outcomes, and provides a foundation for an NCI-funded multicenter randomized diet trial to assess efficacy that is currently underway.

Clinical Trial > Clin Cancer Res. 2025 Jan 17;31(2):316-327. doi: 10.1158/1078-0432.CCR-24-1629.

Re-Irradiation Plus Pembrolizumab: A Phase II Study for Patients with Recurrent Glioblastoma

Fabio M Iwamoto [#1], Shyam K Tanguturi [#2], Lakshmi Nayak [3], Tony J Wang [4], Arati Desai [5], Robert A Lustig [6], Stephen Bagley [5], Eric T Wong [7], Lauren M Hertan [8], Christine McCluskey [3], Julia Hayden [3], Alona Muzikansky [9], Shreya Nakhawa [10], Julia Japo [11], Connor C Bossi [11], Maxime Meylan [10], Ye Tian [10], Graham L Barlow [10], Paul Speliakos [10], Georges Ayoub [11], David M Meredith [11], Keith L Ligon [11], Daphne Haas-Kogan [2], Kun Huang [10], Kai W Wucherpfennig [10], Patrick Y Wen [3], David A Reardon [3]

Affiliations + expand

PMID: 39513953 DOI: 10.1158/1078-0432.CCR-24-1629

Abstract

Purpose: Radiotherapy may enhance antitumor immune responses by several mechanisms, including induction of immunogenic cell death. We performed a phase 2 study of pembrolizumab with re-irradiation in patients with recurrent glioblastoma.

Patients and methods: Sixty patients with recurrent glioblastoma received pembrolizumab with re-irradiation alone (cohort A, bevacizumab-naïve; n = 30) or with bevacizumab continuation (cohort B, n = 30). Dual primary endpoints, including the overall response rate and overall survival (OS) at either 12 (OS-12; cohort A) or 6 months (OS-6; cohort B), were assessed per cohort relative to historic benchmarks. Paired paraffin-embedded formalin-fixed tumor samples were assessed for immunologic biomarkers by IHC using digital quantification and co-detection-by-indexing (CODEX).

Results: Study therapy was well tolerated, with most toxicities being grade ≤3. For cohort B, the primary endpoint of OS-6 was achieved (57%); however, survival was not improved for cohort A patients. The overall response rate was 3.3% and 6.7% for cohorts A and B, respectively. CODEX analysis of paired tumor samples from five patients revealed an increase of activated T cells in the tumor microenvironment after study therapy.

Conclusions: Compared with historic controls, re-irradiation plus pembrolizumab seemed to improve survival among bevacizumab-refractory patients but not among bevacizumab-naïve patients. CODEX revealed evidence of intratumoral infiltration of activated immune effector cells. A randomized, properly controlled trial of PD-1 blockade plus re-irradiation is warranted to further evaluate this regimen for bevacizumab-refractory patients, but alternative approaches are needed for bevacizumab-naïve patients.

> Neurooncol Adv. 2024 Dec 11;7(1):vdae220. doi: 10.1093/noajnl/vdae220. eCollection 2025 Jan-Dec

A phase Ib study evaluating the c–MET inhibitor INC280 (capmatinib) in combination with bevacizumab in patients with high–grade glioma

Gerald S Falchook [1], James D Battiste [2], Amandeep Kalra [3], Mythili Shastry [4], Lindsey Finney [4], Susan J Hoekstra [4], Meredith G Shih [5], Kent C Shih [5 4]

Affiliations + expand

PMID: 39925637 PMCID: PMC11805691 DOI: 10.1093/noajnl/vdae220

Abstract

Background: To improve survival in patients with high-grade glioma, INC280 (capmatinib) a highly selective and potent oral inhibitor of the MET receptor with robust central nervous system (CNS) penetration, was evaluated in combination with bevacizumab (BEV).

Methods: There were 2 phases, dose-escalation (3+3 design) and dose-expansion, which included patients (1) who progressed during or after first-line therapy (no prior BEV), (2) who progressed during or after second-line therapy with BEV, and (3) who had unresectable high-grade glioma (no prior BEV).

Results: Sixty-four patients with high-grade glioma were treated; 18 in escalation cohorts and 46 in expansion Cohorts A (21), B (15), and C (10). The maximum-tolerated dose (MTD) was not reached and the RP2D was 400 mg capmatinib PO BID (800 mg daily). Treatment continued for a median of 14 weeks and up to ~6 years in one patient. Common treatment-related adverse events (65% ≤ Grade 2) included fatigue, peripheral edema, nausea, diarrhea, ALT increased, and constipation. Headaches and seizures occurred in 11 patients; Grade 3+ events included Grade 3 headache (1) and Grade 3 seizures (4). There were no treatment-related deaths. The 12 responders to treatment (2 CRs [1 pt in escalation and 1 pt in Cohort A] and 10 PRs [2 pts in escalation and A = 6, B = 1, and C = 1]) had a median duration of response of 9.2 months. Two patients with durable responses (CR > 5 years, PR > 1 year) did not harbor baseline c-MET alterations.

Conclusion: Capmatinib + BEV was well-tolerated but had no clear signal of activity in c-MET non-activated high-grade glioma.

Meta-Analysis > J Clin Neurosci. 2025 May:135:111138. doi: 10.1016/j.jocn.2025.111138. Epub 2025 Feb 28.

The safety and efficacy of tyrosine kinase inhibitors against EGFR in patients with glioma; A systematic review, meta-analysis, and sub-group analysis on glioblastoma

Mohammad Amin Habibi [1], Muhammad Hussain Ahmadvand [2], Pouria Delbari [3], Mohammad Sina Mirjani [4], Amir Hessam Zare [2], Baran Mehdizadeh [5], Ali Allahdadi [6], Zahra Ardestani [5], Romina Hamidi Rad [7], Aliakbar Aliasgary [8], Saba Sabet [2], Mohammad Shahir Eftekhar [9], Ibrahim Mohammadzadeh [10], Bardia Hajikarimloo [11]

Affiliations + expand

PMID: 40022869 DOI: 10.1016/j.jocn.2025.111138

Abstract

Background: Gliomas, particularly glioblastoma (GBM), remain challenging to treat and have a poor prognosis. Tyrosine kinase inhibitors (TKIs) targeting EGFR have shown promise, but their efficacy in gliomas is not well established. This study aimed to systematically review and meta-analyze the safety and efficacy of EGFR TKIs in patients with glioma, specifically for primary and recurrent GBM.

Methods: A comprehensive literature search was conducted across PubMed, Embase, Scopus, and Web of Science up to January 1, 2024. Randomized controlled trials and observational studies evaluating TKIs in glioma patients were included. Primary outcomes were overall survival (OS), progression-free survival (PFS), and adverse events. A random-effects meta-analysis was performed to pool results. All statistical analysis was performed using STATA v.17.

Results: A total of 2,424 patients from 51 studies were included. The pooled mean OS was 12.68 months (95 % CI: 6.29-19.08) with 1-year and 2-year OS rates of 43 % (95 % CI: 34 %-52 %) and 14 % (95 % CI: 8 %-20 %), respectively. The mean PFS was 9.61 months (95 % CI: 4.83-14.38). The overall response rate was 19 % (95 % CI: 1 %-36 %). Grade ≥ 3 adverse events occurred in 35 % of patients (95 % CI: 13 %-57 %). Subgroup analyses revealed that combination therapies outperformed TKI monotherapy, and some newer TKIs, like vandetanib, showed improved efficacy.

Conclusions: TKIs demonstrate modest but meaningful benefits in glioma treatment, particularly when combined with other therapies. While initial survival improvements are observed, long-term outcomes remain challenging. Further research is needed to develop more potent, brain-penetrant TKIs and optimize combination strategies to improve outcomes in glioma patients.

Clinical Trial > Int J Radiat Oncol Biol Phys. 2025 Sep 1;123(1):84-92.
doi: 10.1016/j.ijrobp.2025.03.043. Epub 2025 Mar 29.

Comprehensive Molecular Analysis in NRG Oncology/RTOG 9813: A Phase 3 Study of Radiation and Temozolomide Versus Radiation and BCNU/CCNU in Anaplastic Astrocytoma

Jessica L Fleming [1], Stephanie L Pugh [2], Susan M Chang [3], Joseph P McElroy [1], Aline P Becker [1], Kenneth D Aldape [4], Helen A Shih [5], Lynn Stuart Ashby [6], Grant K Hunter [7], Jean-Paul Bahary [8], Christopher J Schultz [9], Brian D Kavanagh [10], Vinay K Puduvalli [11], H Ian Robins [12], Maria Werner-Wasik [13], Minesh Mehta [14], Arnab Chakravarti [15]

Affiliations + expand
PMID: 40164352 DOI: 10.1016/j.ijrobp.2025.03.043

Abstract

Purpose: There is a need to better understand the molecular features that characterize grade 3 astrocytomas and their significance in predicting clinical outcomes. The aim of this study was to determine the significance of the 2021 World Health Organization (WHO)-defined molecular subgroups, along with MGMT promoter methylation, and other alterations in NRG Oncology/RTOG 9813.

Methods and materials: Mutation status was determined by immunohistochemistry and/or next-generation sequencing. Copy number alterations and MGMT methylation were determined by Affymetrix Oncoscan and/or Illumina 450K arrays. Progression-free survival and overall survival were estimated using the Kaplan-Meier method and tested using the log-rank test. Multivariable analyses used Cox proportional hazards models.

Results: Application of the 2021 WHO-defined criteria resulted in the reclassification of 26/79 (33%) patients to grade 4 astrocytoma, IDH-mutant or glioblastoma. When looking at newly assigned molecular grade, grade 3 patients experienced longer survival outcomes compared to grade 4 patients. As individual biomarkers, IDH1/2 mutations, MGMT promoter methylation, and ATRX mutations were each associated with longer survival, whereas TERT promoter mutations, EGFR amplification, and gain of chromosome 7/loss of 10 (Chr+7/-10) were associated with shorter survival. Similar survival outcomes were observed for MGMT methylated patients treated with radiation therapy (RT) and temozolomide (TMZ) or RT and BCNU/CCNU, and MGMT unmethylated patients treated with RT and TMZ. Additionally, IDH-mutant patients seemed to respond well to the addition of TMZ.

Conclusions: This study demonstrated the importance of classifying patients according to the 2021 WHO-defined criteria. The majority of IDH-wildtype anaplastic astrocytomas (grade 3) were reclassified as glioblastoma (grade 4). These analyses also shed light on the efficacy of TMZ in certain molecular subgroups, where the addition of TMZ to RT appeared to benefit patients regardless of MGMT methylation status.

> Neurooncol Adv. 2025 Mar 27;7(1):vdaf064. doi: 10.1093/noajnl/vdaf064. eCollection 2025 Jan-Dec.

Integrated early palliative care for patients with newly diagnosed glioblastoma: The GLIOSUPPORT feasibility study

Michel Fabbro [1], Muriel Thomaso [2], Amélie Darlix [3] [1], Virginie Perotin [2], Caroline Gallay [2], Marie Charissoux [4], Anne-Chantal Granier [2], Nabila Bouazza [5], Patrice Champoiral [2], Louise Coutant [2], Marta Jarlier [6], Estelle Guerdoux [7] [2]

Affiliations + expand

PMID: 40351836 PMCID: PMC12063082 DOI: 10.1093/noajnl/vdaf064

Abstract

Background: Early palliative care improves the quality of life (QoL) and survival in patients with cancer; however, its effects in patients with glioblastoma remain unclear. The GLIOSUPPORT study assessed the feasibility (adherence; primary objective) of an early palliative care program integrated into the standard glioblastoma care pathway. Secondary objectives included the description of the patients' characteristics, QoL, and neuropsychological changes over time, end-of-life decisions, end-of-life treatments, and family carers' perceptions/experiences.

Methods: This interventional, prospective, longitudinal, feasibility study was conducted in a French comprehensive cancer center. Thirty-five patients with newly diagnosed glioblastoma were required to reach an adherence rate of 60%. Adherence was defined as going to 3 palliative care visits scheduled every 12 weeks. Baseline characteristics were compared in patients who did and did not adhere to the palliative care program. Minimal clinically important differences and cut-offs were used to quantify QoL changes.

Results: The adherence rate was 60% (95% CI [42.1%-76.1%]), indicating that the program was feasible. Visual disturbances, communication/initiation deficits, and anxiety were more frequent in the group that did not adhere to the program. Emotional and social functioning, pain, appetite loss, constipation, and headache increased over time (clinically significant differences), whereas neuropsychological disturbances did not change. Half of the participants identified a family proxy and 8.6% wrote advance directives. One month before death, 28.6% of patients were receiving cancer treatment.

Conclusions: Integrating early palliative care in glioblastoma management is feasible. The potential benefits on QoL, mood, and survival must now be evaluated in a larger randomized controlled trial.

> Neuro Oncol. 2025 Jul 25:noaf176. doi: 10.1093/neuonc/noaf176. Online ahead of print.

Enhancing Cardiorespiratory Fitness and Quality of Life in High-Grade Glioma through an Intensive Exercise Intervention during Chemotherapy: Proof of Concept

Johanna Jost-Engl [1 2 3], Ralf Ketter [2], Ralf Brandt [1], Klaus Völker [4], Joachim Gerß [5], Kathleen Jetschke [6], Carolin Weiss Lucas [7], Freerk T Baumann [8], Philipp M Lepper [9 10], Steffi Urbschat [2], Walter Stummer [1], Rainer Wiewrodt [3], Dorothee Wiewrodt [1], Mmh Trial Investigators

Affiliations + expand

PMID: 40726159 DOI: 10.1093/neuonc/noaf176

Abstract

Background: High-grade glioma (HGG) patients experience enormous disease burden both from tumor- and treatment-related symptoms. Exercise can improve physical fitness and quality of life (QoL); yet experience in neuro-oncology, especially with high-intensity exercise, remains limited. This study evaluated feasibility, safety, and efficacy of the intensive, structured 16-week strength and endurance program, "Active in Neuro-Oncology" (ActiNO) for HGG patients undergoing chemotherapy.

Methods: In this prospective, oligocentric, single-arm proof-of-concept trial, 54 HGG patients participated in ActiNO, with twice-weekly supervised exercise sessions. The primary endpoint was cardiorespiratory fitness, assessed via physical working capacity (PWC75%) – the workload (W/kg body weight) achieved at 75% of age-adjusted maximum heart rate during a maximal cardiopulmonary exercise test. Secondary endpoints included peak oxygen uptake (VO_2peak), peak power output (Ppeak), and QoL (EORTC QLQ-C30). Analyses focused on within-subject changes from pre-to-post-intervention. Additionally, comparisons to normative data were performed. Feasibility was assessed via accrual, adherence, and attrition; safety via adverse event monitoring (CTCAE).

Results: Program tolerance was high, with few exercise-related adverse events (all CTCAE grade 1-2). Over 16 weeks, significant improvements were observed in PWC75% (1.023 to 1.256 W/kg BW, +23%), VO_2peak (23.04 to 26.09 ml/min/kg BW, +13%), and Ppeak (1.771 to 2.104 W/kg BW, +19%). QoL, including global health and physical functioning, improved, reaching normative values. Adherence was high (85%), though attrition was 48%, mainly due to disease progression or physical constraints.

Conclusions: High-intensity exercise is feasible and safe in HGG patients undergoing chemotherapy. The observed improvements in physical fitness and QoL support incorporating structured exercise into neuro-oncology care.

> Qual Life Res. 2025 Aug;34(8):2405-2418. doi: 10.1007/s11136-025-03984-1. Epub 2025 Jun 5.

Neurocognitive impairment and patient–proxy agreement on health-related quality of life evaluations in recurrent high-grade glioma patients

Ivan Caramanna [1 2], Martin Klein [3 4], Martin van den Bent [5], Ahmed Idbaih [6], Martin J B Taphoorn [7 8], Linda Dirven [7 8], Thierry Gorlia [9], Jaap C Reijneveld [2 9 10 11]; EORTC Quality of Life Group

Affiliations + expand

PMID: 40471413 PMCID: PMC12274216 DOI: 10.1007/s11136-025-03984-1

Abstract

Purpose: The rate of missing data on patient-reported health-related quality of life (HRQOL) in brain tumor clinical trials is particularly high over time. One solution to this issue is the use of proxy (i.e. partner, relative, informal caregiver) ratings in lieu of patient-reported outcomes (PROs). In this study, we investigated patient-proxy agreement on HRQOL outcomes in high-grade glioma (HGG) patients.

Methods: Generic and disease-specific HRQOL was assessed using the EORTC QLQ-C30 and QLQ-BN20 in a sample of 500 patient-proxy dyads participating in EORTC trials 26101 and 26091. Patients were classified as impaired or intact based on their neurocognitive performance. The level of patient-proxy agreement was measured using Lin's concordance correlation coefficient (CCC), and the Bland-Altman limit of agreement. The Wilcoxon signed-rank test was used to evaluate differences between patients' and proxies' HRQOL.

Results: Patient-proxy agreement in all HGG patients (N = 500) ranged from 0.399 to 0.743. Only 18.8% of all patients were neurocognitively intact. Lin's CCC ranged from 0.231 to 0.811 in cognitively impaired patients and their proxies, and from 0.376 to 0.732 in cognitively intact patients and their proxies.

Conclusions: The results of this study suggest that the moderate level of patient-proxy agreement observed in HGG patients would allow reliance on proxies' reports. However, the differences observed between neurocognitively impaired and intact patients stress the importance of taking into consideration patient's clinical and neurocognitive status as well as their mental capacity for adequate clinical decision making in general and for PRO-related issues.

> J Patient Rep Outcomes. 2025 Jan 10;9(1):6. doi: 10.1186/s41687-024-00835-4.

Development of a brief screening measure of unmet supportive care needs (SCNS–P&C–6) in caregivers of people with high–grade glioma

Jill Chen [1], Joanne M Shaw [1], Haryana M Dhillon [2], Georgia K B Halkett [3], Emma McDougall [3], Anna K Nowak [4 5], Rachel Campbell [1]; BRAINs Program Investigators

Affiliations + expand

PMID: 39792320 PMCID: PMC11723857 DOI: 10.1186/s41687-024-00835-4

Abstract

Purpose: Informal caregivers of people with high grade glioma (HGG) often have high levels of unmet support needs. Routine screening for unmet needs can facilitate appropriate and timely access to supportive care. We aimed to develop a brief screening tool for HGG caregiver unmet needs, based on the Supportive Care Needs Survey-Partners & Caregivers (SCNS-P&C).

Methods: Secondary analysis was performed on responses to the SCNS-P&C from 188 HGG caregivers, who participated in the Care-IS trial. SCNS-P&C items were assessed against four criteria: factor loadings; prevalence; variation in domain score; diagnostic accuracy. Supplementary analysis was conducted at two timepoints (T1 & T2) on the final selected items to identify caregivers indicating no needs on the screening items but reported a need on the original SCNS-P&C, suggesting they would be "missed" by the screening items.

Results: Six items performed best against psychometric criteria, capturing two domains: Cancer impact needs and Information and communication needs. Supplementary analysis showed screening items failed to identify only 7.4% (14/188) of caregivers with other unmet needs at T1 and 11.4% (18/158) at T2. Of those missed at T1, only four were missed again at T2.

Conclusions: We identified six-items for inclusion in a brief screening tool, the SCNS–P&C–6, demonstrating good sensitivity in detecting unmet needs of caregivers of people with HGG. Use of this tool in clinical practice has the potential to improve access to care and the cancer experience for both the caregiver and person with brain tumor.

Impact de l'aide sur vie professionnelle et activités habituelles, comprendre l'expérience de personne ayant une tumeur, besoin support émotionnel pour soi, avoir possibilité de discuter de ses préoccupations avec docteur, accès aux informations sur les besoins des malades et accès aux informations sur les besoins des aidants

> Neuro Oncol. 2025 Jul 30;27(6):1519–1535. doi: 10.1093/neuonc/noaf015.

The clinical and molecular landscape of diffuse hemispheric glioma, H3 G34–mutant

Emilie Le Rhun [1 2 3], Andrea Bink [4], Joerg Felsberg [5 6], Dorothee Gramatzki [2], Sebastian Brandner [7 8], Jamal K Benhamida [9], Antje Wick [10 11], Joerg C Tonn [12 13], Malte Mohme [14], Ghazaleh Tabatabai [15 16 17 18], David Capper [19 20], Matija Snuderl [21], Evangelia Razis [22], Michael W Ronellenfitsch [23 24], Nicolas Neidert [25], Ho-Keung Ng [26], Ute Pohl [27], Tejus Bale [9], Stefanie Quach [28 12 13], David Rieger [18], Ulrich Schüller [29 30 31], Julia Onken [32 33 19], Katharina Drüschler [10 11], Claude-Alain Maurage [34], Luca Regli [3], Estelle Healy [35], Maya Graham [36], Tibor Hortobagyi [37], Simon Paine [38], Leslie Bridges [39], Tereza Lausova [40 41], Valentina Medici [4], Philipp Sievers [40 41], David Schrimpf [40 41], Wolfgang Wick [10 11], Felix Sahm [40 41], Guido Reifenberger [5 6], Andreas von Deimling [40 41], Michael Weller [2]

Affiliations + expand

PMID: 39842935 PMCID: PMC12309718 DOI: 10.1093/neuonc/noaf015

Abstract

Background: Diffuse hemispheric glioma, histone 3 (H3) G34-mutant, has been newly defined in the 2021 World Health Organization (WHO) classification of central nervous system tumors. Here we sought to define the prognostic roles of clinical, neuroimaging, pathological, and molecular features of these tumors.

Methods: We retrospectively assembled a cohort of 114 patients (median age 22 years) with diffuse hemispheric glioma, H3 G34-mutant, central nervous system WHO grade 4, and profiled the imaging, histological, and molecular landscape of their tumors.

Results: Compared with glioblastoma, H3 G34-mutant diffuse hemispheric gliomas exhibited less avid contrast enhancement, necrosis, and edema on MRI. Comprehensive analyses of mutational and DNA copy number profiles revealed recurrent mutations in TP53 and ATRX, homozygous deletions of CDKN2A/B, and amplifications of PDGFRA, EGFR, CCND2, and MYCN. MGMT promoter methylation was detected in 79 tumors (75%); 11 tumors (13%) showed DNA copy number profiles suggestive of circumscribed deletions on 10q26.3 involving the MGMT locus. Median survival was 21.5 months. Female sex, gross total resection, and MGMT promoter methylation were positive prognostic factors on univariate analysis. Among radiological, pathological, and molecular features, the absence of pial invasion and the presence of microvascular proliferation and CDK6 amplification were positive prognostic factors on univariate analyses.

Conclusions: This study refines the clinical and molecular landscape of H3 G34-mutant diffuse hemispheric gliomas. Dedicated trials for this novel tumor type are urgently needed.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- **GLIOME DE BAS GRADE**
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> Menopause. 2025 Apr 1;32(4):346-352. doi: 10.1097/GME.0000000000002507.

Association between hormone therapy and glioma risk in US women: a cancer screening trial

Jinyu Pan [1], Chuan Shao [1], Chao Xu [1], Gang Zhang [1], Haotian Jiang [1], Tao Tang [1], Hui Tang [2], Nan Wu [1]

Affiliations + expand

PMID: 39808122 DOI: 10.1097/GME.0000000000002507

Abstract

Objective: Gliomas are the most common primary brain tumors in adults, and the role of hormone therapy (HT) in their development remains controversial. This study with a cohort design aimed to investigate the association between HT use and glioma risk using the data from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

Methods: We analyzed data from 75,335 women, aged 50-78, who were enrolled between 1993 and 2001. The median follow-up period was 11.82 years. Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the relationship between HT use and glioma risk, adjusting for various potential confounders.

Results: Over the follow-up period, 101 participants were diagnosed with glioma. After adjusting for relevant variables, there was no significant association between HT use and glioma risk (HR, 1.16; 95% CI, 0.75-1.81). Similarly, no significant associations were found when considering HT status or duration of use. However, in subgroup analysis by education, marital status, body mass index, oral contraceptive, hysterectomy, ovariectomy, ever been pregnant, age at menarche, and age at menopause, we found that a significant positive association was only observed in the group with at least college graduate (HR, 3.00; 95% CI, 1.02-8.84). The interaction effect for education was not significant (P = 0.056).

Conclusions: Our findings suggest no overall link between HT use and glioma risk. Further research is needed to confirm these results.

Review > Brain Sci. 2025 Aug 21;15(8):894. doi: 10.3390/brainsci15080894.

Optic Pathway Glioma: Current Treatment Approaches and Ongoing Clinical Trials

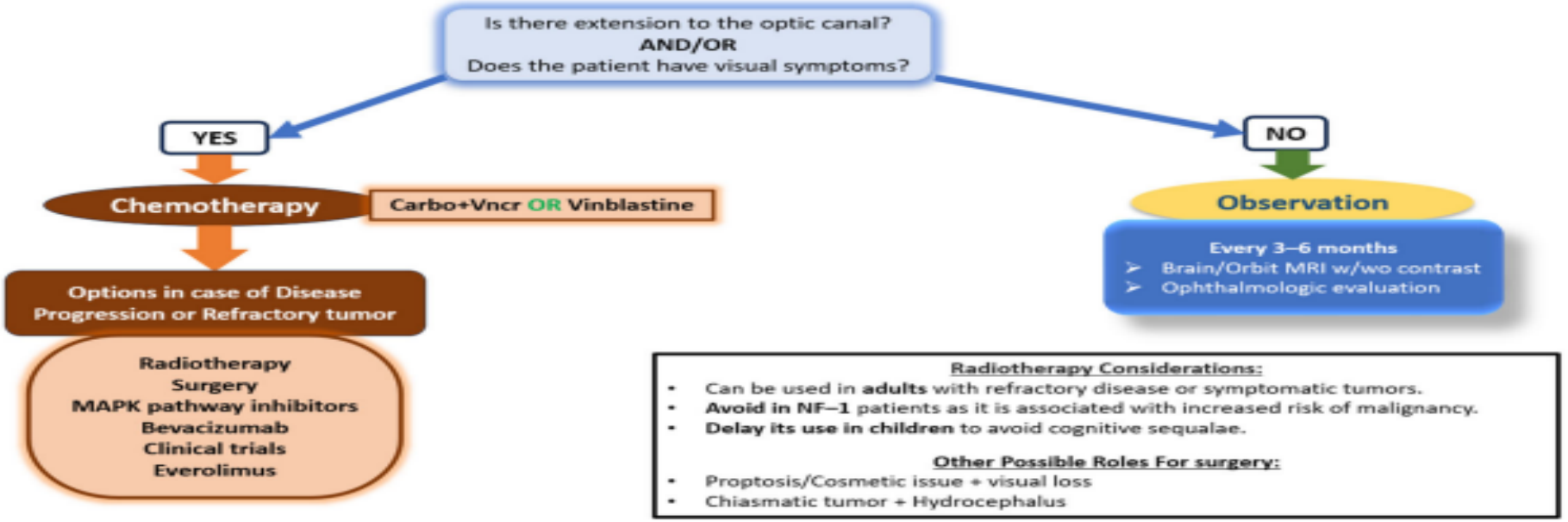
Osama Elzaafarany [1], Sarah Elhomosany [2], Alexandra Rincones [3], Vincent Dlugi [1], Sepideh Mokhtari [1]

Affiliations + expand

PMID: 40867225 PMCID: PMC12385051 DOI: 10.3390/brainsci15080894

Abstract

Optic pathway glioma (OPG) is a rare pediatric low-grade glioma, frequently associated with neurofibromatosis type 1 (NF-1), that presents unique therapeutic challenges due to its anatomical location and its potential to impair vision, endocrine function, and developmental trajectories. Current clinical management prioritizes a multidisciplinary, patient-specific approach aimed at tumor control while preserving long-term quality of life. Strategies vary based on clinical presentation, ranging from observation in asymptomatic cases to chemotherapy for progressive or symptomatic tumors. Surgical and radiation options are limited due to potential risks and complications. In recent years, advances in molecular characterization have guided the development of targeted therapies, particularly MEK inhibitors, which demonstrate encouraging efficacy and reduced toxicity profiles. In parallel, investigational therapies including immunotherapy and precision medicine-based approaches are under clinical evaluation. This review provides a synthesis of current standard practices, emerging targeted treatments, and ongoing clinical trials, drawing on relevant literature and expert consensus to inform clinicians and families about available therapeutic options. Literature discussed in this review was identified through a non-systematic search of published articles, clinical trial registries, and authoritative guidelines, with selection based on relevance, clinical significance, and contribution to understanding current and emerging management strategies for OPG.



> Acta Neuropathol. 2025 Feb 2;149(1):11. doi: 10.1007/s00401-025-02846-x.

MSH2, MSH6, MLH1, and PMS2 immunohistochemistry as highly sensitive screening method for DNA mismatch repair deficiency syndromes in pediatric high-grade glioma

Lea L Friker [1 2], Thomas Perwein [3 4], Andreas Waha [5], Evelyn Dörner [5], Rebecca Klein [5], Mirjam Blattner-Johnson [6 7], Julian P Layer [8 9], Dominik Sturm [6 7 10], Gunther Nussbaumer [3], Robert Kwiecien [11], Isabel Spier [12 13], Stefan Aretz [12 13], Kornelius Kerl [14], Ulrike Hennewig [15], Marius Rohde [15], Axel Karow [16 17], Ingmar Bluemcke [18], Ann Kristin Schmitz [19], Harald Reinhard [19], Pablo Hemáiz Driever [20], Susanne Wendt [21], Annette Weiser [22 23], Ana S Guerreiro Stücklin [22 23], Nicolas U Gerber [22], André O von Bueren [24 25], Claudia Khurana [26], Norbert Jorch [26], Maria Wiese [27], Christian P Kratz [28], Matthias Eyrich [29], Michael Karremann [30], Ulrich Herrlinger [31], Michael Hölzel [8], David T W Jones [6 7], Marion Hoffmann [27], Torsten Pietsch [5], Gerrit H Gielen [# 5], Christof M Kramm [# 27]

Affiliations + expand

PMID: 39894875 PMCID: PMC11788232 DOI: 10.1007/s00401-025-02846-x

Abstract

Pediatric high-grade glioma (pedHGG) can occur as first manifestation of cancer predisposition syndromes resulting from pathogenic germline variants in the DNA mismatch repair (MMR) genes MSH2, MSH6, MLH1, and PMS2. The aim of this study was to establish a generalized screening for Lynch syndrome and constitutional MMR deficiency (CMMRD) in pedHGG patients, as the detection of MMR deficiencies (MMRD) may enable the upfront therapeutic use of checkpoint inhibitors and identification of variant carriers in the patients' families. We prospectively enrolled 155 centrally reviewed primary pedHGG patients for MMR-immunohistochemistry (IHC) as part of the HIT-HGG-2013 trial protocol. MMR-IHC results were subsequently compared to independently collected germline sequencing data (whole exome sequencing or pan-cancer DNA panel next-generation sequencing) available in the HIT-HGG-2013, INFORM, and MNP2.0 trials. MMR-IHC could be successfully performed in 127/155 tumor tissues. The screening identified all present cases with Lynch syndrome or CMMRD (5.5%). In addition, MMR-IHC also detected cases with exclusive somatic MMR gene alterations (2.3%), including MSH2 hypermethylation as an alternative epigenetic silencing mechanism. Most of the identified pedHGG MMRD patients had no family history of MMRD, and thus, they represented index patients in their families. Cases with regular protein expression in MMR-IHC never showed evidence for MMRD in DNA sequencing. In conclusion, MMR-IHC presents a cost-effective, relatively widely available, and fast screening method for germline MMRD in pedHGG with high sensitivity (100%) and specificity (96%). Given the relatively high prevalence of previously undetected MMRD cases among pedHGG patients, we strongly recommend incorporating MMR-IHC into routine diagnostics.

> Neurooncol Adv. 2024 Dec 19;7(1):vdae224. doi: 10.1093/noajnl/vdae224. eCollection 2025 Jan-Dec.

Clinical value of the *MGMT* promoter methylation score in IDHmt low-grade glioma for predicting benefit from temozolomide treatment

Amélie Darlix [1] [2], Pierre Bady [3] [4] [5], Jérémy Deverdun [6] [7], Karine Lefort [8], Valérie Rigau [9] [1], Emmanuelle Le Bars [6] [7], Justine Meriadec [6], Mathilde Carrière [6], Arthur Coget [6], Thomas Santarius [10], Tomasz Matys [11], Hugues Duffau [12] [1], Monika E Hegi [13] [5]

Affiliations + expand

PMID: 40041202 PMCID: PMC11877643 DOI: 10.1093/noajnl/vdae224

Abstract

Background: Diffuse IDH mutant low-grade gliomas (IDHmt LGG) (World Health Organization grade 2) typically affect young adults. The outcome is variable, with survival ranging from 5 to over 20 years. The timing and choice of initial treatments after surgery remain controversial. In particular, radiotherapy is associated with early and late cognitive toxicity. Over 90% of IDHmt LGG exhibit some degree of promoter methylation of the repair gene O(6)-methylguanine-DNA methytransferase (*MGMTp*) that when expressed blunts the effect of alkylating agent chemotherapy, for example, temozolomide (TMZ). However, the clinical value of *MGMTp* methylation predicting benefit from TMZ in IDHmt LGG is unclear.

Methods: Patients treated in the EORTC-22033 phase III trial comparing TMZ versus radiotherapy served as training set to establish a cutoff based on the MGMT-STP27 methylation score. A validation cohort was established with patients treated in a single-center first-line with TMZ after surgery/surgeries.

Results: The MGMT-STP27 methylation score was associated with better progression-free survival (PFS) in the training cohort treated with TMZ, but not radiotherapy. In the validation cohort, an association with next treatment-free survival ($P = .045$) after TMZ was observed, and a trend using RANO criteria ($P = .07$). A cutoff value set above the 95% confidence interval of being methylated was significantly associated with PFS in the TMZ-treated training cohort, but not in the radiotherapy arm. However, this cutoff could not be confirmed in the test cohort.

Conclusions: While the *MGMTp* methylation score was associated with better outcomes in TMZ-treated IDHmt LGG, a cutoff could not be established to guide treatment decisions.

> Front Oncol. 2025 Jan 20:14:1445558. doi: 10.3389/fonc.2024.1445558. eCollection 2024.

Hippocampus-sparing volume-modulated arc therapy in patients with World Health Organization grade II glioma: a feasibility study

Renxian Xie [1] [2], Hongxin Huang [1] [2], Qingxin Cai [1], Jiayang Lu [1], Tong Chen [1] [2], Keyan Xie [2], Jianzhou Chen [1], Chuangzhen Chen [1]

Affiliations + expand

PMID: 39902134 PMCID: PMC11788287 DOI: 10.3389/fonc.2024.1445558

Abstract

Background: Radiotherapy can improve the survival rates of patients with glioma; meanwhile, impaired cognitive functions have been brought to the forefront with the offending organ, the radiosensitive hippocampus. This study aimed to assess the feasibility of hippocampus-sparing volumetric-modulated arc therapy (HS VMAT) in patients with World Health Organization (WHO) grade II glioma.

Methods: HS VMAT plans and non-hippocampus-sparing volumetric-modulated arc therapy (NHS VMAT) plans were generated using a computed tomography (CT) dataset of 10 patients who underwent postoperative radiotherapy. The dose volume histogram (DVH), homogeneity index (HI), conformity index (CI), and irradiated dose of the hippocampus and other organs at risk (OARs) were analyzed.

Results: No significant differences were observed in HI and CI between the two plans. Regarding the protection of OARs, HS VMAT plans were equally capable and even lowered the radiation dosages to the brainstem (35.56 vs. 41.74 Gy, $p = 0.017$) and spinal cord (1.34 vs. 1.43 Gy, $p = 0.006$). Notably, HS VMAT plans markedly decreased doses to the ipsilateral hippocampus and the contralateral hippocampus, demonstrating its efficacy in hippocampal dose reduction.

Conclusion: The HS VMAT plan can be used to efficiently lower the dosage delivered to the hippocampus and may, to some extent, help lessen the risk of cognitive damage. The encouraging results of our study need to be further validated by clinical trials to confirm the benefits of the HS VMAT plans in preserving cognitive functions in patients with glioma.

Multicenter Study > Radiat Oncol. 2025 Aug 5;20(1):124. doi: 10.1186/s13014-025-02702-y.

Proton therapy for adult type IDH-mutated glioma: Proglio-1, a multicenter retrospective study

Nicolas Goliot [1 2], Emmanuel Jouglar [3 4 5], Julian Jacob [6], François Christy [7], Eva Seutin [8], Renaud Schiappa [8], Sarah Dumont [9], Selim Mohssine [10 11], Dinu Stefan [10], Arthur Leclerc [11 12], Evelyne Emery [11 12], Cyril Moignier [10], Jeanne Riverain [10], Fernand Missohou [10], Maxime Fontanilles [13 14], Samuel Valable [11], Jacques Balosso [10], Jérôme Doyen [15], Paul Lesueur [10 11 16]

Affiliations + expand

PMID: 40764578 PMCID: PMC12326604 DOI: 10.1186/s13014-025-02702-y

Abstract

Background: Gliomas with isocitrate dehydrogenase (IDH) mutation affect young adults with a long-life expectancy. While radiotherapy is effective, studies have shown its detrimental effects on cognition and quality of life. Unlike photon radiotherapy, proton therapy better spares healthy tissue. This study aimed to report mid-term survival and toxicities of proton therapy in a multicentric cohort of adults with IDH-mutant gliomas.

Methods: We retrospectively analyzed 90 patients treated with proton therapy in France since 2016, including 60 with IDH-mutated astrocytomas and 30 with oligodendrogliomas. Overall survival (OS) and progression-free survival (PFS) were estimated by Kaplan-Meier and compared with the log-rank test. Prognostic factors were assessed using univariate Cox models. Toxicities, radiation-induced-contrast-enhancement (RICE) and patterns of recurrence were evaluated.

Results: At the time of proton therapy, World Health Organization (WHO) pathology grades 2, 3, and 4 were observed in 42%, 54%, and 3% of patients, respectively. Protons were delivered as upfront therapy in 41 patients and after recurrence in 49. After a median follow-up of 27.3 months, median OS was not reached, and median PFS was 42.5 months for the whole cohort. WHO grades 3-4 had lower PFS than WHO grade 2 ($p = 0.044$). Patterns of recurrence were in-field (79%), out-of-field (7%), borderline (4%), and mixed (11%). Proton therapy was well tolerated, with only three grade > 2 toxicities. RICE occurred in 23 patients, but 74% of them did not require any treatment.

Conclusions: Proton therapy in IDH-mutated gliomas shows a favorable mid-term tolerance and efficacy profile.

> Neuro Oncol. 2025 Jul 12:noaf165. doi: 10.1093/neuonc/noaf165. Online ahead of print.

RANO seizure working group–Tumor Related Epilepsy Assessment Tool (RANO–TREAT) to assess seizure control for glioma treatment trials and clinical practice

Edward K Avila [1], Anne S Reiner [1], Terri S Armstrong [2], Ashley E Aaroe [3], Elizabeth M Cunningham [4], Julie G Brown [5], Francesco Bruno [6], Jose Diarte [1], Aya Haggiagi [7], Rebecca A Harrison [8], Adela Joanta-Gomez [9], Johan A F Koekkoek [10], Eudocia Q Lee [11], Emilie Le Rhun [12], Hope Miller [2], Katherine S Panageas [1], Edwin N Peguero [5], Roberta Ruda [6], Riccardo Soffietti [6], Jessica W Templer [4], Steven Tobochnik [13], Elizabeth Vera [2], Michael A Vogelbaum [5], Michael Weller [12], Martin van den Bent [14]

Affiliations + expand

PMID: 40650343 DOI: 10.1093/neuonc/noaf165

Abstract

Background: No standardized method exists for seizure assessment in glioma clinical trials. We describe the development and evaluation of RANO-TREAT (Tumor Related Epilepsy Assessment Tool) for seizure assessment and its association with changes on brain MRI.

Methods: Patients with glioma/glioneuronal tumors and ≥1 prior seizure along with clinicians completed RANO-TREAT in conjunction with brain MRIs, yielding multiple RANO-TREAT scores at clinic visits over time. Unweighted (primary) and weighted (post-hoc) scores were correlated with disease progression via MRI in all patients and patients with IDHmt tumors, separately. Cohorts were randomly split by patient into cohort-specific training and validation sets. Weights for RANO-TREAT items were defined by multivariable generalized estimating equation models in cohort-specific training sets and validated in cohort-specific validation sets. A nomogram was developed using overall cohort training and validation sets.

Results: 490 patients (310 IDHmt tumors) had ≥1 visits and 285 patients (168 IDHmt tumors) had ≥2 visits. Unweighted RANO-TREAT scores (OR:1.01; 95%CI:0.998-1.02; P=0.13) and score changes (OR:1.00; 95%CI:0.99-1.02; P=0.63) were not associated with progressive disease on MRI. Post-hoc analysis using training and validation sets demonstrated weighted RANO-TREAT scores were correlated with progressive disease in both overall cohort validation set (OR:2.51; 95%CI:1.80-3.52; P<0.0001) and IDHmt cohort validation set (OR:4.53; 95%CI:2.11-9.75; P=0.0001). Weighted analyses for patients with ≥2 visits showed similar associations in validation sets.

Conclusions: This prospective study suggests an association of seizure control evaluated by a new standardized tool with disease progression in glioma. This tool requires further systematic evaluation in glioma clinical trials alongside more traditional endpoints.

Meta-Analysis > Anticancer Drugs. 2025 Oct 1;36(9):749-758.

doi: 10.1097/CAD.0000000000001746. Epub 2025 Jul 21.

Effect of valproic acid and levetiracetam administration on the survival of glioma patients: a meta-analysis study

Arya Shirani [1], Mobin Obeidinia [1], Makan Ziafati [1], Javad Garavand [2], Moazzameh Ramezani [3], Fatemeh Ramezani [4]

Affiliations + expand

PMID: 40699178 DOI: 10.1097/CAD.0000000000001746

Abstract

In this meta-analysis study, the effect of valproate (VPA) and levetiracetam (LEV) on the survival of glioma patients taking temozolomide (TMZ) was investigated. The cumulative hazard ratios (HR) of overall survival (OS) and progression-free survival from published clinical studies were determined using a random effects model to estimate the strength of the association between VPA/LEV and survival in glioma patients. The results showed that VPA (data from 2304 patients from 14 clinical trial studies) and LEV (data from 1610 patients from 11 clinical trial studies) increase OS by 20% [HR = 0.80; 95% confidence interval (CI), 0.69-0.94; P = 0.01] and 18% (HR = 0.82; 95% CI, 0.68-0.98; P = 0.03), respectively. Use of VPA and LEV as anticonvulsant drugs increased the OS of patients with glioma taking TMZ to an almost equal extent. These findings need to be confirmed in larger prospective studies.

> J Neurooncol. 2025 Feb;171(3):659-668. doi: 10.1007/s11060-024-04888-9. Epub 2024 Dec 16.

Health-related quality of life in 62 patients with diffuse low-grade glioma during a non-therapeutic and progression-free phase: a cross-sectional study

Tiphaine Obara [1 2], Marie Blonski [3 4], Marie Forest-Dodelin [3 4], Fabien Rech [4 5], Luc Taillandier [3 4]

Affiliations + expand

PMID: 39680337 PMCID: PMC11729205 DOI: 10.1007/s11060-024-04888-9

Abstract

Purpose: Few studies have evaluated the health-related quality of life (HRQoL) of patients with diffuse low-grade glioma (LGG) during a clinical and radiological monitoring period. We report a cross sectional cohort study of HRQoL in patients with LGG and compare the results with normative population data. We then explore factors associated with HRQoL.

Methods: We used the European Organisation for Research and Treatment of Cancer QLQ-C30, BN-20 and the Hospital Anxiety and Depression Scale (HADS) to evaluate HRQoL. Averaged QLQC30 and HADS scores were compared with scores of a normative population. A general linear model multivariate analysis of variance was used to investigate the association between HRQoL and independent factors.

Results: A total of 62 patients with LGG completed HRQoL questionnaires. Compared with a normative population, LGG patients reported statistical and clinically significant lower cognitive, emotional, role and social functioning. Fatigue, anxiety, depression and sleep disturbances were frequently reported. Awake surgery and preserved high Karnofsky Performance Status were found to be independent prognostic factors for better global HRQoL, while radiotherapy was associated with worsened HRQoL.

Conclusion: Despite a non-therapeutic and progression free phase, LGG patients report noticeable limitations in several HRQoL subscales. Our study highlights the importance of HRQoL assessment not only at diagnosis or during active therapeutic stage. Further studies are needed to develop better adapted tools of HRQoL assessment.

Clinical Trial > Neuro Oncol. 2025 Jun 21;27(5):1341–1355. doi: 10.1093/neuonc/noae274.

Radiographic and visual response to the type II RAF inhibitor tovorafenib in children with relapsed/refractory optic pathway glioma in the FIREFLY–1 trial

Karsten Nysom [1], Lindsay B Kilburn [2], Sarah E S Leary [3], Daniel B Landi [4], Evelien de Vos-Kerkhof [5], Sébastien Perreault [6], Olaf Witt [7 8 9 10 11], David S Ziegler [12 13 14], Pablo Hernáiz Driever [15], Andrea T Franson [16], Patricia A Baxter [17], Nicholas S Whipple [18], Cassie Kline [19], Devorah Segal [20], Nada Jabado [21], Simon Bailey [22], Geoffrey McCowage [23], Jordan R Hansford [24 25 26], Dong-Anh Khuong-Quang [27], Nicholas G Gottardo [28 29], Timothy Hassall [30], Jung Woo Han [31], Michal Yalon Oren [32], Susan N Chi [33], Jiaheng Qiu [34], Daniel Da Costa [34], Sandya Govinda Raju [34], Peter Manley [34], Darren Hargrave [35]

Affiliations + expand

PMID: 39700439 PMCID: PMC12187376 DOI: 10.1093/neuonc/noae274

Abstract

Background: Due to their anatomical locations, optic pathway gliomas (OPGs) can rarely be cured by resection. Given the importance of preserving visual function, we analyzed radiological and visual acuity (VA) outcomes for the type II RAF inhibitor tovorafenib in the OPG subgroup of the phase 2 FIREFLY-1 trial.

Methods: FIREFLY-1 investigated the efficacy (arm 1, n = 77), safety, and tolerability (arms 1/2) of tovorafenib (420 mg/m2 once weekly; 600 mg maximum) in patients with BRAF-altered relapsed/refractory pediatric low-grade glioma (pLGG). In this post hoc analysis, anti-tumor activity and VA were analyzed in arm 1 patients with OPG. Anti-tumor activity was independently assessed per Response Assessment in Neuro-Oncology high-grade glioma (RANO-HGG), Response Assessment in Pediatric Neuro-Oncology-LGG (RAPNO), and RANO-LGG criteria. The data cutoff was June 5, 2023.

Results: Forty-two of 77 patients had OPGs; 35 of 42 had ≥2 VA assessments. The overall response rate in the OPG subgroup according to RANO-HGG, RAPNO, and RANO-LGG criteria were 64%, 50%, and 55%, with clinical benefit rates of 95%, 88%, and 90%, respectively. VA per patient was preserved for 80% of patients; 31% demonstrated improved VA; VA per eye was preserved in 87%, with 27% improving. The safety profile in the arm 1 OPG subgroup was similar to the overall FIREFLY-1 safety analysis set.

Conclusions: Tovorafenib demonstrated anti-tumor activity in relapsed/refractory BRAF-altered OPG across radiological assessment criteria and was generally well tolerated. Importantly, vision remained stable or improved in most patients.

Clinical Trial > Clin Cancer Res. 2025 Apr 14;31(8):1383-1389.

doi: 10.1158/1078-0432.CCR-24-3439.

FDA Approval Summary: Tovorafenib for Relapsed or Refractory BRAF-Altered Pediatric Low-Grade Glioma

Sonia Singh [1], Diana Bradford [1], Somak Chatterjee [1], Xiaoxue Li [1], Stephanie L Aungst [1], Amy M Skinner [1], Claudia P Miller [1], Sarah Kim-McOlash [1], Jeanne Fourie Zirkelbach [1], Ye Xiong [1], Youwei Bi [1], Ying-Hong Wang [1], Yuching Yang [1], Jielin Sun [1], Jeffrey Kraft [1], Rosane Charlab [1], Stacy S Shord [1], Shenghui Tang [1], Barbara Scepura [1], Ilynn Bulatao [1], Opeyemi Udoka [1], Haleh Saber [1], Nam Atiqur Rahman [1], Richard Pazdur [1 2], Harpreet Singh [1 2], Martha Donoghue [2], Nicole Drezner [1]

Affiliations + expand

PMID: 39808502 PMCID: PMC11996598 (available on 2025-10-14)

DOI: 10.1158/1078-0432.CCR-24-3439

Abstract

On April 23, 2024, the FDA granted accelerated approval to tovorafenib, a type II RAF kinase inhibitor, for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (pLGG) harboring a BRAF fusion or rearrangement or BRAF V600 mutation. Efficacy was evaluated in FIREFLY-1 (NCT04775485), a single-arm, open-label, multicenter trial that enrolled patients 6 months to 25 years of age with relapsed or refractory pLGG with an activating BRAF alteration who had received prior systemic therapy. The major efficacy outcome measure was the radiologic overall response rate, defined as the proportion of patients with complete response, partial response, or minor response as determined by blinded independent central review using Response Assessment in Pediatric Neuro-Oncology criteria. A key secondary endpoint was duration of response. In an efficacy population of 76 patients, the overall response rate was 51% (95% confidence interval, 40-63), and the median duration of response was 13.8 months (95% confidence interval, 11.3-not estimable). The required postmarketing clinical trial (FIREFLY-2) was well underway at the time of accelerated approval. This represents the first FDA approval of a systemic therapy for the treatment of patients with pLGG with BRAF fusions or rearrangements.

Meta-Analysis > World Neurosurg. 2025 Jan:193:447-460. doi: 10.1016/j.wneu.2024.10.071. Epub 2024 Nov 14.

Efficacy and Safety of Bevacizumab Combined with Temozolomide in the Treatment of Glioma: A Systematic Review and Meta-Analysis of Clinical Trials

Chuheng Wang [1], Linan Duan [1], Yao Zhao [1], Yubo Wang [1], Yunqian Li [2]

Affiliations + expand

PMID: 39461419 DOI: 10.1016/j.wneu.2024.10.071

Abstract

Objective: Glioma is the most common malignant brain tumor in neurosurgery. Bevacizumab (BEV) is a monoclonal antibody that inhibits tumors by inhibiting vascular endothelial growth factor and reducing tumor angiogenesis. To evaluate the efficacy and safety of BEV combined with temozolomide (TMZ) in glioma, we performed a meta-analysis.

Methods: PubMed, Embase, The Cochrane Library, and Web of Science databases were searched for randomized controlled trials comparing survival outcomes between TMZ combined with BEV and TMZ alone as well as cohort studies were included in our study. The primary outcome measures analyzed were overall survival (OS) and progression-free survival (PFS).

Results: A total of 6 randomized controlled trials and 4 cohort studies with a total of 2515 patients were included in our meta-analysis. The results of meta-analysis suggested that there were no significant improvements in overall survival, but the combination of TMZ and BEV prolonged progression-free survival, improved overall response rate, and increased the incidence of some adverse reactions, compared with TMZ alone. Subgroup analysis suggested sex, recursive partitioning analysis grade, O-6-methylguanine-DNA methyltransferase gene status and radiotherapy combination did not affect the improvement of OS with the combination of the 2 drugs, and recursive partitioning analysis grade did not affect the improvement of PFS with the combination of the 2 drugs.

Conclusions: The combination of TMZ and BEV can improve PFS as well as overall response rate in patients and has no benefit on OS. At the same time, the adverse reactions during the combination of the 2 drugs were acceptable.

> Neuro Oncol. 2025 Apr 17:noaf065. doi: 10.1093/neuonc/noaf065. Online ahead of print.

A Phase 2 PBTC Study of Selumetinib for Recurrent/Progressive Pediatric Low-Grade Glioma: Strata 2, 5, and 6 with Long-term Outcomes on Strata 1, 3, and 4

Jason Fangusaro [1], Arzu Onar-Thomas [2], Tina Young Poussaint [3], Shelly Lensing [2], Azra H Ligon [4], Neal Lindeman [5], Anuradha Banerjee [6], Lindsay B Kilburn [7], Alicia Lenzen [8], Natasha Pillay-Smiley [9], Ian F Pollack [10], Nathan J Robison [11], Sonia Partap [12], Ibrahim Qaddoumi [2], Daniel Landi [13], David T W Jones [14], Clinton F Stewart [2], Maryam Fouladi [15], Ira J Dunkel [16]

Affiliations + expand

PMID: 40241281 DOI: 10.1093/neuonc/noaf065

Abstract

anti-MEK ciblant voie NF1

Background: PBTC-029B was a phase 2 trial evaluating efficacy of selumetinib in children with recurrent/progressive low-grade glioma. We report results of strata 2, 5, and 6 with updated survivals for strata 1, 3, and 4.

Methods: Stratum 2 included recurrent/progressive pilocytic astrocytoma (PA) not associated with neurofibromatosis type-1 (NF1) that screened negative for the BRAF-KIAA1549 fusion and BRAFV600E mutation. Stratum 5 enrolled non-PA that screened positive for one of the BRAF aberrations. Stratum 6 enrolled children who consented to tissue screening, but there was an assay failure. For long-term survivals, stratum 1 included non-NF1 PA positive for one of the BRAF aberrations; stratum 3 included NF1-associated pLGG; and stratum 4 included non-NF1 optic pathway/hypothalamic tumors.

Results: Stratum 2: among 14 evaluable patients, there was 1 partial response (PR), 7 stable disease (SD) and 6 progressive disease (PD); overall response rate (ORR) was 7.1%. Two-year progression-free survival (PFS)/overall survival (OS) were 57.1%/100%, respectively. Stratum 5: among 23 evaluable patients, there was 1 complete response (CR), 4 PR, 12 SD, and 6 PD; ORR was 21.7%. Two-year PFS/OS were 74.8%/100%, respectively. Stratum 6: among 26 evaluable patients, there were 7 PR, 14 SD, and 5 PD; ORR was 26.9%. Two-year PFS/OS were 72.0%/100%, respectively. The median follow-up for patients on strata 1, 3, and 4 without events are 60.4, 60.4, and 58.1 months, and 5-year PFS/OS were 30.8%/88.9%, 54.2%/100%, and 51.0%/100%, respectively.

Conclusions: Selumetinib provided stability and responses across many pLGG subgroups, and some patients achieved prolonged disease control without additional therapy.

> J Neurooncol. 2025 May;172(3):695-703. doi: 10.1007/s11060-025-04961-x. Epub 2025 Mar 5.

Impact of pregnancy on the treatment and outcomes of glioma: a cohort study

Jack M Shireman [1], Emily Distler [1], Cheyenne Schepp [1], Yilong Tao [1], Liam McCarthy [1], Varshitha Kasulabada [1], Mahua Dey [2]

Affiliations + expand

PMID: 40042713 DOI: 10.1007/s11060-025-04961-x

Abstract

Background: Pregnancy's impact on cancer has been understudied throughout the literature. The current authoritative cancer database in the US, NCI's SEER database, tracks nearly all aspects of cancer care however has no provision to track pregnancy. Consequently, there are no systematic evidence based clinical guidelines available for this vulnerable population.

Objective: This retrospective cohort study outlines reported clinical presentation, obstetric outcomes, and treatment regimens for pregnant patients diagnosed with glioma to better understand current practice pattern for glioma during pregnancy.

Evidence review: An exhaustive PubMed and Cochrane based literature search was performed for pregnancy and glioma. Individual patient data was extracted primarily from case reports and case series, since pregnancy is an exclusion criterion for most clinical trials.

Findings: We identified a cohort of 94 patients, 54% of whom (n = 51/94) were diagnosed prior to their pregnancy. Of the patients who were diagnosed during their pregnancy, diagnosis was most common in the second trimester (27%, n = 25/94). Seizure was the most common presenting symptom and maternal survival varied significantly by glioma grade. Treatment delays were common and were most detrimental to maternal survival in glioblastoma (GBM) (22 months (no delay) vs 8 months (delay) $p < 0.10$). Most patients regardless of tumor grade delivered healthy babies (80%, n = 75/94) while GBM carried the highest rate of birth complications or defects (15% n = 3/20). Fetal exposure to chemotherapy and/or radiotherapy increased the rate of birth defects or complications from 5% (n = 2/47) to 16% (n = 6/37).

Conclusions and relevance: In summary, we found wide practice variation in management of glioma during pregnancy. Systematic reporting on this vulnerable population is needed to better serve mothers and fetuses during this incredibly challenging life event.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- **GLIOME DE LA LIGNE MEDIANE et du TRONC**
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Multicenter Study > Eur J Cancer. 2025 Feb 5:216:115165. doi: 10.1016/j.ejca.2024.115165. Epub 2024 Dec 11.

Real life data of ONC201 (dordaviprone) in pediatric and adult H3K27-altered recurrent diffuse midline glioma: Results of an international academia-driven compassionate use program

D Di Carlo [1], M Annereau [2], M Vignes [2], L Denis [2], N Epaillard [3], S Dumont [3], D Guyon [3], A Rieutord [2], S Jacobs [4], V Salomon [5], I Yoldjian [5], F Duperray [5], L Brunel [5], X Baiao [6], F Lemos [7], E Vauleon [8], M Capra [9], S Abbou [10], M Touat [11], M Sanson [11], V Gandemer [12], E De Carli [13], F Bourdeaut [14], I Hezam [15], G Vassal [15], J Grill [10]

Affiliations + expand

PMID: 39700833 DOI: 10.1016/j.ejca.2024.115165

Abstract

Introduction: H3K27-altered diffuse midline gliomas (DMG) have limited therapeutic options and a very poor prognosis. Encouraging responses were observed in early clinical trials with ONC201. As ONC201 was unavailable in Europe, a compassionate use program supported by the French Authorities was launched for patients at progression after standard of care radiotherapy.

Methods: This program was developed by the French Society of Pediatric Oncology (SFCE) and Association des Neuro-Oncologues d'Expression Française in collaboration with the French National Agency For Medicines and Health Products Safety and Parents Associations.

Results: 174 patients (102 children, 72 adults) from 14 countries were treated from November 2021 to August 2023 at Gustave Roussy Institut (Villejuif, France). 37 % received a second course of irradiation at the time of relapse. Median duration of treatment was 57 days or 1,9 months (mo) (range 1-456 days). Median OS since diagnosis for the whole cohort was 466 days or 15,5 mo (112-2612 days); 426 or 14,2 mo (112-2612 days) and 590 or 19,6 mo (range 160-1881) for children and adults, respectively (p = 0.001). Median OS after ONC201 start was 143 days or 4,7 mo (1-711 days) for the whole cohort. Univariate and multivariable analysis identified site (thalamus) and age (older) as favorable prognostic factors. Reirradiation was associated with significantly longer survival after ONC201 start only in children.

Conclusion: While the efficacy of ONC201 needs validation in a controlled randomized clinical trial, our real-life data support a better outcome for patients with thalamic tumors treated with ONC201. We demonstrated furthermore the feasibility of a successful academia-driven compassionate use program.

> Am J Cancer Res. 2025 Jun 15;15(6):2701-2718. doi: 10.62347/MXZH5646. eCollection 2025.

The therapeutic potential of repurposed mebendazole, alone and in synergistic combination with ONC201, in the treatment of diffuse midline glioma

Serena Gentile [1], Federica Toma [2], Donatella Lucchetti [2 3], Lucia Lisi [4], Pierluigi Navarra [4], Alessandro Sgambato [2 3], Tiziana Servidei [1], Antonio Ruggiero [1 5]

Affiliations + expand

PMID: 40667566 PMCID: PMC12256405 DOI: 10.62347/MXZH5646

Abstract

H3K27-altered diffuse midline glioma (DMG) is a universally fatal disease with no available therapeutic strategies apart from palliative radiotherapy. Repurposing marketed non-cancer drugs in oncology is emerging as a fast-tracking approach to speed up the development of new treatment options, urgently needed for DMG. Repurposed anthelmintic mebendazole (MBZ) is in the spotlight against brain tumors, because it joins promising anticancer properties with high neuropenetrance, favorable pharmacokinetic and safety profile. Although MBZ is undergoing Phase I/II trials against brain tumors, including DMG, MBZ anticancer properties and the underlying mechanisms of actions have poorly been characterized in DMG preclinical models. We found that MBZ robustly reduced cell viability in six out of seven DMG cell lines with either K27M-mutated or wild-type H3. All IC_{50} values (range 102 to 958 nM) fell in a clinically attainable range. The antiproliferative MBZ properties were mediated by an arrest of DMG cells in the G_2/M phase with a concomitant upregulation of the key cell cycle regulators p21 and p27, whereas p53 upregulation and activation were cell context-dependent. At the same growth-inhibitory concentrations, MBZ triggered apoptotic cell death, as evidenced by higher levels of the apoptotic markers caspase-3 and PARP cleavage. Consistently, Annexin V-Propidium iodide (PI) double staining showed MBZ dose-dependent increase in both stages of apoptosis. Of interest, the combination of MBZ with the first-in-class imipridone ONC201 sinergistically increased the antiproliferative effects in two DMG cell lines as assessed by combination scores with different algorithms, showing additive effects in two others cell lines. Mechanistically, the combination potentiated the proapoptotic activity of either MBZ or ONC201, while not changing the cytokinetic perturbations induced by the single drugs. Finally, one pair of ONC201-sensitive and ONC201-resistant DMG cell lines with acquired resistance showed same responsiveness to MBZ with similar values of IC_{50} and E_{max}. In conclusion, MBZ demonstrates high growth-inhibitory/proapoptotic activity, chemosensitization property to ONC201 and the ability to overcome ONC201 resistance in DMG cell cultures, proposing as a new low-toxicity therapeutic for DMG, with a potential to be used in second-line treatment and/or in combination protocols.

Clinical Trial > Pediatr Blood Cancer. 2025 May;72(5):e31619. doi: 10.1002/pbc.31619. Epub 2025 Feb 25.

Phase I Study of Vorinostat and Temsirolimus in Newly Diagnosed or Progressive Diffuse Intrinsic Pontine Glioma

Lea M Stitzlein [1,2], Muhammad Usman Baig [3], Joya Chandra [1,2,4], Suzanne McGovern [5], Arnold Paulino [5], Leena M Ketonen [6], Soumen Khatua [7], Wafik Zaky [1,8]

Affiliations + expand

PMID: 40000388 DOI: 10.1002/pbc.31619

Abstract

Background: Diffuse intrinsic pontine glioma (DIPG) carries a poor prognosis with a median survival of less than 12 months. Key molecular features include histone H3 mutation (K27M) and AKT pathway dysregulation. There is currently no curative treatment.

Methods: This is a Phase I study of vorinostat and temsirolimus in newly diagnosed (Stratum 1) and progressive (Stratum 2) DIPG (NCT02420613). The primary aims are to determine the safety, maximum tolerated dose (MTD), and toxicities. A modified 3 + 3 design was used to establish the MTD, where the first three patients were assigned the first dose level regardless of stratum. Stratum 1 received radiotherapy with vorinostat, followed by up to 10 cycles of vorinostat and temsirolimus. Stratum 2 received up to 12 cycles of vorinostat and temsirolimus. Vorinostat was administered at a fixed dose of 230 mg/m^2 daily on Days 1-8, and temsirolimus was administered on Days 1 and 8 at 25 mg/m^2 (Dose level 1) or 35 mg/m^2 (Dose level 2).

Results: Six patients were enrolled, three in each stratum. No dose-limiting toxicity was observed, and most adverse effects were limited to Grades 1 or 2, including fatigue, myelosuppression, hyperlipidemia, hyperglycemia, elevated creatinine, nausea, vomiting, and headache. One patient experienced Grade 3 leukopenia. In the study, the MTD with acceptable toxicity was vorinostat 230 mg/m^2 and temsirolimus 35 mg/m^2.

Conclusions: Overall, the combination of temsirolimus and vorinostat is well-tolerated and safe, prompting the need for larger studies to investigate its efficacy.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- **ASTROBLASTOME**
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Case Reports > J Neurosurg Pediatr. 2025 May 30;36(3):360-368. doi: 10.3171/2025.2.PEDS24426. Print 2025 Sep 1.

Primary spinal cord astroblastoma: a case report and systematic review of the literature detailing management and understanding histopathological, epigenetic, and molecular analysis

Adam Y Li [1], Tharan Mungara [1], Aman Singh [1], Anna C Kolstad [1], Catherine Jay [1], Rajnish Bharadwaj [2], David A Paul [1], Melissa A LoPresti [1], David N Korones [3], Howard J Silberstein [1]

Affiliations + expand

PMID: 40446351 DOI: 10.3171/2025.2.PEDS24426

Abstract

Objective: Astroblastomas (ABs) are rare glial tumors categorized by MN1 gene alterations in the WHO 2021 CNS tumor guidelines. While previously reported primarily in cerebral hemispheres, there have been few reports regarding primary spinal ABs, and no established guidelines have been published on the management of these lesions. Here, the authors present an illustrative case with a systematic review exploring presenting characteristics, diagnosis, management, and outcomes of spinal AB.

Methods: The patient's electronic medical record was retrospectively reviewed. Additionally, a systematic literature review was performed by searching the PubMed, Cochrane Library, Embase, and Web of Science databases for articles published through June 20, 2024, and all English-language articles describing patients with primary spinal AB were analyzed. Conference abstracts and articles describing secondary spinal AB or cerebral AB were excluded. Eleven previous cases of primary spinal AB were identified. Articles were screened by multiple reviewers to limit bias. For each case, clinical presentation, surgical pathology, molecular testing, treatment strategies, clinical course, and outcome were tabulated and compared.

Results: A 6-year-old male presented with thoracic back pain and limp and was found to have a high-grade thoracic AB with EWSR1::BEND2 fusion, treated with resection and radiation therapy; he is clinically stable at 12 months of follow-up. A systematic review yielded 11 prior cases; patient ages ranged from 3 months to 36 years, with most cases being pediatric. Clinical presentations commonly featured back pain, motor weakness, and gait disturbances. All cases except one underwent resection. Common pathological findings included perivascular hyalinization, pseudorosettes, pseudopapillae, high cellularity, and positive staining for glial fibrillary acidic protein/epithelial membrane antigen/S100. Molecular testing showed direct MN1 alteration in 6 cases, while the remaining cases showed MN1 methylation, EWSR1::BEND2 fusion, and MAMLD1::BEND2 fusion. Eight patients underwent chemotherapy, and 7 underwent radiation therapy. Except for 2 reported deaths, most patients were alive at the last follow-up (range 1 month-15 years). Progression of spinal AB occurred in one-third (4/12) of cases.

Conclusions: With the present report of a patient whose tumor exhibited EWSR1::BEND2 fusion, there are now 12 total reports in the literature of primary spinal AB. These cases span various pathological and molecular testing results, treatment strategies, and clinical courses. Given the diversity of current molecular signatures of spinal AB, this summative assessment of the current literature offers insights to inform guidelines for classifying AB and developing evidence-based treatment strategies going forward.

Review > Neuropathology. 2025 Aug;45(4):e70016. doi: 10.1111/neup.70016. Epub 2025 Jun 3.

Low-Grade Primary Intramedullary Spinal Cord Astroblastoma: A Case Report and Literature Review

Irfan Kesumayadi [1], Atsushi Kambe [1], Tetsuji Uno [1], Tomohiro Hosoya [1], Karen Makishima [2], Makoto Sakamoto [1], Kurosaki Masamichi [1]

Affiliations + expand

PMID: 40462495 DOI: 10.1111/neup.70016

Abstract

Spinal astroblastoma is an exceedingly rare entity characterized by features that overlap with other spinal cord tumors. We present a case of a 67-year-old male who presented with trunk dysesthesia, motor weakness, and progressive hypoesthesia in both lower limbs. Magnetic resonance imaging (MRI) revealed edematous changes in the spinal cord at the C6-Th1 level on T2-weighted sequences, with a centrally enhancing lesion at the C7 level on gadolinium-enhanced T1-weighted imaging. Consistent with previous reports, spinal astroblastomas frequently involve the cervical and thoracic regions. Pathological examination in our case revealed pseudopapillary cellular arrangements surrounding hyalinized microvasculature. Immunohistochemical analysis demonstrated retained INI1/SMARCB1 expression and mixed-origin features, with positive staining for EMA, GFAP, OLIG2, neurofilament, and synaptophysin. The tumor exhibited low-grade characteristics, with no mitotic activity, necrosis, or significant MIB-1 index (0.3%), and followed a gradual clinical course. Genetic profiling revealed no MN1 alteration or fusion genes. Based on these findings, a diagnosis of low-grade spinal astroblastoma, not elsewhere classified, was made. In conclusion, spinal astroblastoma should be considered in the differential diagnosis of primary intramedullary spinal cord tumors, particularly those located in the cervicothoracic region and exhibiting mixed-origin features. The sharing of cases among clinicians is crucial for enhancing awareness and understanding of this rare pathology.

Review > Childs Nerv Syst. 2025 Feb 14;41(1):112. doi: 10.1007/s00381-025-06768-7.

Posterior fossa astroblastoma: a case report of an extremely rare tumor with challenging diagnosis in a child and a review of literature

Ehab Shabo [1], Saida Zoubaa [2], Gerrit H Gielen [2], Ralf Clauberg [3], Christian Wispel [4], Torsten Pietsch [2], Hartmut Vatter [5], Sevgi Sarikaya-Seiwert [4]

Affiliations + expand

PMID: 39953192 PMCID: PMC11828785 DOI: 10.1007/s00381-025-06768-7

Abstract

A 7-year-old boy presented to the hospital with recurrent nausea and vomiting over 2 weeks. A cranial MRI revealed a large heterogeneous lesion in the posterior fossa extending from the fourth ventricle to the foramen magnum with contact to the brainstem. The lesion showed moderate diffusion restriction and multiple small cystic components. The child underwent gross total resection. The primary histological findings suggested proliferative active tumor without further definition. The extended histological examination 3 weeks later confirmed the diagnosis of astroblastoma. Due to complete resection and full recovery of the patient, watchful waiting with radiological follow-up was recommended. Astroblastoma is an extremely rare tumor especially in the posterior fossa. However, it should be considered as a differential diagnosis in every tumor presenting the discussed radiological and histological features, especially in young aged patients.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- **XANTHOASTROCYTOME**
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> Neurooncol Adv. 2025 Jul 19;7(1):vdaf089. doi: 10.1093/noajnl/vdaf089. eCollection 2025 Jan-Dec.

Molecular, histologic, and clinical characterization of methylation class pleomorphic xanthoastrocytoma: An analysis of 469 tumors

Christopher H Dampier [1], Niharika Shah [1], Kristyn Galbraith [2], Azadeh Ebrahimi [3], Osorio Lopes Abath Neto [4], Zied Abdullaev [1], Sanda Alexandrescu [5], Felipe Andreiuolo [6 7 8], Terri Armstrong [9], Tiffany Baker [10], Sahara Cathcart [11], Hye-Jung Chung [1], Patrick J Cimino [12], Kyle S Conway [13], Jennifer Cotter [14], Felipe D'Almeida Costa [15], Karen Dazelle [1], Nima Etminam [16], Sima Esther Ferman [17], Igor Fernandes [18], Christina K Ferrone [1], Ahmed Gilani [19], Mark Gilbert [9], Jason Gregory [20], Courtney Ketchum [1], Han Sung Lee [21], Ina Lee [1], Maria Beatriz S Lopes [22], Qinwen Mao [23], Michael S Marshall [24], Matthew McCord [25], Stewart G Neill [26], Jeffrey J Nirschl [27], Byram H Ozer [9], Werner Paulus [28], Marta Penas-Prado [9], Marco Prinz [29 30], Peter Pytel [31], Martha Quezado [1], Mark Raffeld [1], Sharika Rajan [1], Miriam Ratliff [16], Guido Reifenberger [32], Lorraina Robinson [23], Jens Schittenhelm [3], Daniel Schrimpf [33], Omkar Singh [1], Christian Thomas [28], Diana Thomas [34], Jaiyeola Thomas-Ogunniyi [35], Angus Toland [19], Rust Turakulov [1], Rachael Vaubel [36], Nitin Wadhwani [37], Jing Wu [9], Caterina Giannini [36 38], Matija Snuderl [2], Sebastian Brandner [39], Andreas von Deimling [33], Kenneth Aldape [1]

Affiliations + expand

PMID: 40735274 PMCID: PMC12305539 DOI: 10.1093/noajnl/vdaf089

Abstract

Background: Methylation class pleomorphic xanthoastrocytoma (mcPXA) comprises tumors with the DNA methylation signature of classical PXA but with a wider histologic spectrum, including overlap with glioblastoma (GBM).

Methods: To clarify the histologic and molecular scope of mcPXA and characterize its clinical behavior, a cohort of 469 tumor samples from 458 patients matching to mcPXA by the DKFZ classifier (v12.6 score ≥0.85) was interrogated.

Results: Patient median age was 23 years (range 1-73 years) with a female predominance (259 female/199 male). *CDKN2A/B* homozygous deletion was observed in 406 of 469 (87%) samples. In samples tested for *BRAF* p.V600E mutations (n = 279), 240 (86%) harbored the mutation. A chr7+/chr10- pattern was observed in 103 of 469 (22%) samples. Among samples tested for *TERT* promoter mutations (n = 143), 32 (22%) harbored the mutation. Progression-free and overall survival of patients with mcPXA were comparable to patients with methylation class IDH-mutant astrocytoma, low grade, but a GBM-like subset (ie, cases with a pre-methylation working diagnosis of GBM) showed shorter survival. Histologic features of high grade, including palisading necrosis and microvascular proliferation, were prognostic in mcPXA. Compared to patients with *BRAF* p.V600E-altered GBM, patients with mcPXA were younger and had a lower frequency of *TERT* promoter mutations.

Conclusion: Tumors in mcPXA share molecular characteristics with histologically defined PXA, and high-grade histologic features can help predict their clinical behavior. The use of an epigenetic classification of PXA reveals that this group of tumors is more common than previously appreciated and warrants in-depth study to identify efficacious therapeutic options.

Case Reports > Front Oncol. 2025 Mar 31:15:1527909. doi: 10.3389/fonc.2025.1527909. eCollection 2025.

Case Report: SMARCB1–deficient phenotype may be a new specialized type of pleomorphic xanthoastrocytoma associated with poor prognosis

Hui Zhang [1], Xueping Xiang [2], Xiaojing Ma [2], Buyi Zhang [1], Susu Xu [1], Xiaojuan He [1], Jinghong Xu [1]

Affiliations + expand

PMID: 40231261 PMCID: PMC11994728 DOI: 10.3389/fonc.2025.1527909

Abstract

Pleomorphic xanthoastrocytoma (PXA) is a rare, localized glioma characterized by frequent *BRAF* V600E mutations and *CDKN2A/B* deletions. Compared to *IDH*-wildtype glioblastoma, PXA has a better prognosis. Recently, rare cases of PXA with rhabdoid histological characteristics have been reported, which are titled atypical teratoid/rhabdoid tumor arising in a PXA. However, the genetic characteristics of these cases have rarely been investigated. Herein, we present a 49-year-old woman with a mass in the left frontotemporal region. Microscopically, this mass is composed of the glial and rhabdoid elements, both of which have molecular features of PXA, and the rhabdoid elements assessed using immunohistochemistry for SMARCB1 (INI1) expression demonstrated expression loss. The DNA methylation profile showed a significant calibrated score of 0.81 for methylation class PXA. The tumor was eventually diagnosed as a PXA with SMARCB1 deficiency.

Observational Study > Neurosurgery. 2025 Feb 1;96(2):416-425.
doi: 10.1227/neu.0000000000003083. Epub 2024 Jun 28.

Pleomorphic Xanthoastrocytoma: Multi-Institutional Evaluation of Stereotactic Radiosurgery

Ali Haluk Düzkalir [1], Yavuz Samanci [1 2], Ahmed M Nabeel [3 4], Wael A Reda [3 5], Sameh R Tawadros [3 5], Khaled Abdelkarim [3 6], Amr M N El-Shehaby [3 5], Reem M Emad [3 7], Nuria Martínez Moreno [8], Roberto Martínez Álvarez [8], David Mathieu [9], Ajay Niranjan [10], L Dade Lunsford [10], Zhishuo Wei [10], Regan M Shanahan [10], Roman Liscak [11], Jaromir May [11], Antonio Dono [12], Angel I Blanco [12], Yoshua Esquenazi [12], Samantha Dayawansa [13], Jason Sheehan [13], Manjul Tripathi [14], Matthew J Shepard [15], Rodney E Wegner [16], Rituraj Upadhyay [17], Joshua D Palmer [17], Selcuk Peker [1 2]

Affiliations + expand

PMID: 38940575 DOI: 10.1227/neu.0000000000003083

Abstract

Background and objectives: Pleomorphic xanthoastrocytoma (PXA) is a rare low-grade glial tumor primarily affecting young individuals. Surgery is the primary treatment option; however, managing residual/recurrent tumors remains uncertain. This international multi-institutional study retrospectively assessed the use of stereotactic radiosurgery (SRS) for PXA.

Methods: A total of 36 PXA patients (53 tumors) treated at 11 institutions between 1996 and 2023 were analyzed. Data included demographics, clinical variables, SRS parameters, tumor control, and clinical outcomes. Kaplan-Meier estimates summarized the local control (LC), progression-free survival, and overall survival (OS). Secondary end points addressed adverse radiation effects and the risk of malignant transformation. Cox regression analysis was used.

Results: A total of 38 tumors were grade 2, and 15 tumors were grade 3. Nine patients underwent initial gross total resection, and 10 received adjuvant therapy. The main reason for SRS was residual tumors (41.5%). The median follow-up was 34 months (range, 2-324 months). LC was achieved in 77.4% of tumors, with 6-month, 1-year, and 2-year LC estimates at 86.7%, 82.3%, and 77.8%, respectively. Younger age at SRS (hazard ratios [HR] 3.164), absence of peritumoral edema (HR 4.685), and higher marginal dose (HR 6.190) were significantly associated with better LC. OS estimates at 1, 2, and 5 years were 86%, 74%, and 49.3%, respectively, with a median OS of 44 months. Four patients died due to disease progression. Radiological adverse radiation effects included edema (n = 8) and hemorrhagic change (n = 1). One grade 3 PXA transformed into glioblastoma 13 months after SRS.

Conclusion: SRS offers promising outcomes for PXA management, providing effective LC, reasonable progression-free survival, and minimal adverse events.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- **EPENDYMOME**
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Int J Cancer. 2025 Nov 15;157(10):2114-2123. doi: 10.1002/ijc.70016. Epub 2025 Jun 23.

How long should survivors of pediatric medulloblastoma and ependymoma be screened for recurrence? A retrospective cohort study

Thomas F C Meulendijks [1 2 3], Gertjan J L Kaspers [4 5], Vijay Ramaswamy [1 6], Derek S Tsang [1 2 6], Suzanne Laughlin [6 7], Julie Bennett [1 8], Paul C Nathan [1 6]

Affiliations + expand

PMID: 40548641 DOI: 10.1002/ijc.70016

Abstract

Recurrence is the most common cause of late mortality in pediatric brain tumor survivors. However, it is unclear how long such patients should be monitored with periodic neuroimaging. Therefore, we investigated the utility of neuroimaging surveillance for recurrence ≥5 years post diagnosis in survivors of pediatric medulloblastoma and ependymoma. We conducted a retrospective study of survivors of medulloblastoma or ependymoma treated between 2000 and 2017. Eligible survivors were disease-free 5 years after diagnosis and underwent magnetic resonance imaging surveillance ≥5 years after diagnosis. Medulloblastoma survivors with a history of recurrence <5 years after diagnosis were excluded. Of 302 children diagnosed in the study period, 129 met inclusion criteria (89 medulloblastoma/40 ependymoma; 77 (59.7%) male; median age at diagnosis 6 years (range < 1-13); median time from diagnosis to last scan 134 months (61-283)). Four medulloblastoma patients had late recurrent disease, one of which was detected on routine neuroimaging (asymptomatic). All medulloblastoma patients with late recurrence died, except for one previously unirradiated patient who was disease-free 29 months after recurrence. Nine ependymoma patients had late recurrence of which 7 were detected on routine neuroimaging. Six out of seven asymptomatic late recurrent ependymoma patients remain alive with a median time after recurrence of 45.5 months (range: 3-121). Both symptomatic patients died. Among ependymoma survivors, asymptomatic detection of late recurrence by surveillance neuroimaging was associated with better survival than symptomatic detection, supporting the continuation of surveillance for at least 10 years after diagnosis. The benefit of prolonged surveillance in medulloblastoma survivors remains uncertain.

> Turk Neurosurg. 2025;35(2):285-292. doi: 10.5137/1019-5149.JTN.46386-24.2.

The Effect of Initial Treatment Modality on Oncological Outcomes in Children with Ependymoma

Caglayan Esen [1], Pantea Bayatfard, Gozde Yazici, Guzide Burca Aydin, Figen Soylemezoglu, Berrin Babaoglu, Tezer Kutluk, Faruk Zorlu

Affiliations + expand

PMID: 40129206 DOI: 10.5137/1019-5149.JTN.46386-24.2

Abstract

Aim: To evaluate the oncological outcomes and the prognostic factors for children with ependymoma who receive radiotherapy (RT) ± chemotherapy after surgery.

Material and methods: The medical records of 71 children with ependymoma who received RT between 2001 and 2022 were retrospectively evaluated. Survival outcomes and prognostic factors were analyzed using log-rank and cox-regression tests. SPSS v24.0 was utilized for statistical analyses.

Results: Gross total resection (GTR) was achieved in 37 (52%) patients. Craniospinal fluid (CSF) seeding was observed in 8 (11%) patients at the time of diagnosis. The median RT dose was 54 Gy (42-60 Gy). The median time from surgery to the first RT was 2.4 months (1-109 months). The median follow-up time was 65.9 months (2.5-242.8 months), and 5-y overall survival, progression-free survival (PFS), and local recurrence-free survival (LRFS) were 74%, 39%, and 46%, respectively. Recurrence was observed in 41 (58%) patients. Among patients who initiated treatment with chemotherapy, 5-y PFS and LRFS were higher in patients who received RT at the time of diagnosis than those who received RT at the progression (23% vs. 0%, $p < 0.001$ and 39% vs 0%, $p < 0.001$). In multivariate analysis, increased time from surgery to radiotherapy was found to be a poor prognostic factor for PFS.

Conclusion: Young age, less than GTR, large residual tumor volume, initiation of treatment with chemotherapy after surgery, and increased time from surgery to radiotherapy may deteriorate survival. RT should not be delayed until progression, even in young patients receiving chemotherapy.

› Eur Spine J. 2025 Feb;34(2):665-674. doi: 10.1007/s00586-024-08601-2. Epub 2024 Dec 10.

PRO-QOL after gross total resection of spinal ependymoma: a retrospective study based on 3-year follow-up observations in a single center

Dingbang Chen [# 1], Tianxiang Shao [# 1 2], Haocheng Zhu [# 1], Xin Gao [1], Quan Huang [1], Xinghai Yang [3], Qi Jia [4], Jianru Xiao [5]

Affiliations + expand

PMID: 39653854 DOI: 10.1007/s00586-024-08601-2

Abstract

Background: Although many studies have reported clinical outcomes of spinal ependymoma (SE) patients after gross total resection (GTR), the data about the patient reported outcomes of the quality of life (PRO-QOL) was limited.

Purpose: This study investigated the recovery process of PRO-QOL and explored the possibility of predicting the recovery of postoperative QOL by preoperative clinical indicators.

Methods: A retrospective analysis was performed in 71 SE patients who underwent GTR in our center from 2016 to 2022. The PRO-QOL data were collected by questionnaire, which included the EuroQol 5-Dimensions 5-Levels (EQ-5D-5 L) scale and visual pain analogue score (VAS). Factors affecting postoperative PRO-QOL deterioration was assessed by the univariate and multivariate analyses.

Results: 71 SE patients who undergone GTR were included and followed by mean of 36 months (range 27-58). The overall PRO-QOL recovered to a stable level 6 months after surgery, but the ability of self-care, as one of the dimensions of QOL, continued to improve up to one year after surgery. 21 (29.6%) patients reported that their QOL became worse at one year after surgery. The result of statistical analysis suggested that preoperative Modified McCormick Scale (MMS), the number of segments involved by the tumor and preoperative VAS score were identified as main preoperative variables for predicting QOL deterioration.

Conclusion: From the perspective of PRO-QOL, neurological rehabilitation should be continued for at least 6-12 months after GTR to the SE patients. For the preoperative patients with severe neurological damage, long-level intraspinal tumor and low VAS score, more cautious surgical considerations, more perioperative attention and earlier neurological intervention are necessary.

Observational Study › Clin Neurol Neurosurg. 2025 Feb:249:108758. doi: 10.1016/j.clineuro.2025.108758. Epub 2025 Jan 26.

Characteristics and therapeutic profile of the patients with upper cervical spinal cord ependymoma from the medulla oblongata to C4: A cohort of 108 cases

Haiyue Lin [1], Xing-Yu Chen [1], Shixin Gu [1], Xiaodong Liu [1], Wentao Gu [1], Xiaoming Che [1], Jianlan Zhao [2], Rong Xie [3]

Affiliations + expand

PMID: 39889612 DOI: 10.1016/j.clineuro.2025.108758

Abstract

Background: Upper cervical spinal ependymomas (uCSE) is routinely identified as intramedullary ependymomas located from the oblongata medulla to C4 level. Our study aimed to report the outcomes and treatment profiles of uCSE from our cohort of uCSE patients.

Methods: This retrospective observational study included 108 patients with upper cervical spinal ependymomas (uCSE) who underwent surgery at Huashan Hospital from 2008 to 2022. Demographic and clinical data were collected to identify risk factors may associated with post-operative spinal cord function, quality of life and respiratory function.

Results: The mean age of included patients was 44.30 ± 12.71 years old. The most common uCSE was ependymoma (103 of 108, 95.37 %), followed by subependymoma (3 of 108, 2.78 %) and anaplastic Ependymoma (2 of 108, 1.85 %). Age (P = 0.003), sex (P = 0.004), duration of symptoms (P = 0.010), pre-operative bladder functions (P = 0.012), post-operative pneumonia (P = 0.013) and Carbon Dioxide Retention (CDR) (P = 0.004) could independently correlate with living quality of uCSE patients. Post-operative spinal cord function was associated with pneumonia immediately after operation (P = 0.017). In addition, post-operative pneumonia correlated with tumor location (P = 0.048), pre-operative McCormick scores (P = 0.008)/ motor functions (P = 0.022)/ NRS scores (P = 0.020), and tracheotomy immediately after operation (P < 0.001). Tracheotomy immediately after operation was associated with tumor location (P = 0.023), unsteady walking (P = 0.033), pre-operative NRS scores (P = 0.029), post-operative pneumonia (P < 0.001) and CDR (P < 0.001).

Conclusion: Within uCSE patients, post-operative quality of life is associated with pre-operative spinal cord function and symptom duration, which emphasizing the importance of early intervention. Their post-operative respiratory dysfunctions also correlated with post-operative spinal cord function and quality of life.

Global Spine J. 2025 May;15(4):1905-1913. doi: 10.1177/21925682241270101. Epub 2024 Nov 1.

Development and Validation of a Predictive Nomogram for Patients With Myxopapillary Ependymoma: A Surveillance, Epidemiology, and End Results (SEER) Retrospective Cohort Analysis

Abhishek S Bhutada [1 2 3], Srijan Adhikari [1 2 3], Joshua A Cuoco [1 2 3], Austin R Hoggarth [1 2 3], Vaibhav M Patel [1 2 3], Adeolu L Olasunkanmi [1 2 3]

Affiliations + expand

PMID: 39485724 PMCID: PMC11559927 DOI: 10.1177/21925682241270101

Abstract

Study DesignRetrospective Study.ObjectiveMyxopapillary ependymomas (MPEs) are a unique subgroup of spinal ependymomas originating from the filum terminale's ependymal glia. The 2021 WHO classification reclassified all MPEs as grade 2, recognizing their higher recurrence risk. Due to their rarity, our objective with this study is to understand MPEs' clinical course and optimal management through a large retrospective cohort analysis.MethodsFrom the years 2000 to 2020, patients with MPEs were identified from the Surveillance, Epidemiology, and End Results (SEER) database. Univariate and multivariable Cox proportional hazard models were run to identify variables that had a significant impact on the primary endpoint of overall survival (OS). A predictive nomogram was built to predict 5-year and 10-year survival probability.ResultsThis retrospective cohort includes 1373 patients. Patients 65 years or older at diagnosis had a poorer OS ($P < 0.001$). Most patients received subtotal resection. Only 320 patients (23%) received gross total resection (GTR). Patients that received GTR had the best OS when compared against all other modalities of treatment ($P < 0.05$). Receiving radiotherapy did not affect OS in patients with MPE ($P = 0.2$). Nomogram includes patient age and treatment modalities, demonstrating acceptable accuracy in estimating the survival probability at 5-year and 10-year intervals, with a C-index of 0.80 (95% CI of 0.71 to 0.90).ConclusionThis study highlights the survival benefit of GTR in the treatment of patients with MPE. The role of adjuvant radiotherapy remains unclear as it did not seem to improve OS. The nomogram stratifies the risk of survival in patients with MPE based on age and treatment modality.

Clin Neurol Neurosurg. 2025 Mar:250:108807. doi: 10.1016/j.clineuro.2025.108807. Epub 2025 Feb 19.

Geriatric patients undergo surgery less and have worse survival outcomes with intramedullary ependymoma: A surveillance, epidemiology, and end results database analysis

Taylor Furst [1], Muhammad I Jalal [2], Prasanth Romiyo [2], Suyash Sau [2], Jonathan Stone [2], Tyler Schmidt [2]

Affiliations + expand

PMID: 39983522 DOI: 10.1016/j.clineuro.2025.108807

Abstract

Objective: Intramedullary ependymomas account for ~50 % of all primary tumors in the spinal cord. Though gross total resection has become mainstay, other predictors of survival remain poorly characterized. The present study aims to perform a survival analysis and compare prognostic factors across pediatric, adult and geriatric cohorts.

Methods: The Surveillance, Epidemiology, and End Results database was employed to isolate cases of intramedullary ependymomas from 2000 to 2021. Cases were grouped based on age: 0-19 years=pediatric, 20-64 years=adult, 65 + years=geriatric. Kaplan Meier followed by multivariate cox regression analyses were used to identify survival trends. Univariate comparison analyses compared age cohorts.

Results: 2045 cases were included. Geriatric patients demonstrate increased risk of mortality (pediatric vs geriatric: HR=0.23, CI [0.13-0.39], $p < 0.001$; adult vs geriatric: HR=0.18, CI [0.15-0.23], $p < 0.001$). Compared to adult patients (92.7 %), geriatric patients (85.2 %) underwent significantly less surgery ($p < 0.001$). Sex did not influence pediatric or geriatric survival nor did surgery statistically impact pediatric survival, but otherwise surgery not performed, male patients and grade III tumors significantly worsened overall and age-specific survival. Surgery performed in a pediatric patient led to a longer mean survival of 19.8 months, which is clinically relevant despite not meeting statistical significance. Year of diagnosis did not impact overall ($p = 0.79$) nor age-specific survival (pediatric: $p = 0.98$, adult: $p = 0.91$, geriatric: $p = 0.11$).

Conclusions: Geriatric patients suffer from worse survival than those of younger age. Surgery decreases mortality, yet less geriatric patients are receiving surgical resection. No significant survival gains have been made over the last two decades among any age. Further study is needed to optimize medical management to compliment surgical resection and surgery should be considered more often in geriatric patients to improve survival.

> J Neurosurg Case Lessons. 2025 Jun 23;9(25):CASE25146. doi: 10.3171/CASE25146. Print 2025 Jun 23.

Recurrent parietal lobe supratentorial ependymoma, ZFTA fusion–positive, CNS WHO grade 3, with new dural and calvarial reactive changes in a child: illustrative case

Justin N Passman [1], Emily Bellow [1], Heshwin Singh [1], Robert S Kleyner [1], Roberta Seidman [2], David A Chesler [1] [3]

Affiliations + expand

PMID: 40550208 PMCID: PMC12184531 DOI: 10.3171/CASE25146

Abstract

Background: Supratentorial ependymoma, ZFTA fusion-positive, CNS WHO grade 3, is a rare pediatric brain tumor characterized by brisk mitotic activity and sometimes microvascular proliferation and/or necrosis. Typical treatment includes a combination of resection, chemotherapy, and radiation therapy. These tumors often present at age 3 or 4 years and have a poor prognosis.

Observations: The authors present the case of a 4-year-old girl who presented asymptomatically with recurrence of a supratentorial ependymoma, ZFTA fusion-positive, CNS WHO grade 3, of the right parietal lobe with a homozygous CDKN2A deletion through chemotherapy after an initial gross-total resection. Tumor recurrence presented with a traditional intraparenchymal cystic component that initially appeared to invade through the dura mater, diploë, and outer table of the skull. On closer examination of the calvaria and dura in the operating room, a trabeculated and soft tissue mixed with invasion into the outer table contiguous with calcifications on the native dura was observed. Histopathological analysis confirmed that the recurrent tumor was confined intradurally with treatment effect, and the dural and calvarial findings represented a reactive inflammatory process likely related to prior surgery, chemotherapy, and possibly the neoplasm itself.

Lessons: This case illustrates an atypical presentation of a recurrent supratentorial ependymoma, ZFTA fusion-positive, CNS WHO grade 3, where reactive inflammatory changes of the dura and calvaria mimicked dural and calvarial invasion. These findings demonstrate the importance of histopathological evaluation in distinguishing true tumor recurrence from atypical inflammatory responses to prior surgery, chemotherapy, or the neoplasm itself and close postoperative follow-up.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- **Tumeur des PLEXUS CHOROIDES**
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> J Neurooncol. 2025 Oct;175(1):333-343. doi: 10.1007/s11060-025-05136-4. Epub 2025 Jun 26.

CPT-SIOP registry: evaluation of risk factors for disease progression in pediatric choroid plexus papilloma

Christian Fiedler [1], Uwe R Kordes [1], Christian Thomas [2], Martin Hasselblatt [2], Brigitte Bison [3], Lars Behrens [3], Martin Mynarek [1 4], Rolf-Dieter Kortmann [5], Beate Timmermann [6], Torsten Pietsch [7], Jenny Adamski [8], Johannes E A Wolff [9], Stefan Rutkowski [1], Denise Obrecht-Sturm [10]

pediatric A : supratentorial, low-risk paediatric tumors (histological CPP and aCPP;
B: supratentorial, high-risk pediatric tumors (histological CPP, aCPP and CPC°
Adult: infratentorial, low-risk tumors predominantly effecting adult patients (histological CPP and aCPP, "adult")

Purpose: Choroid plexus papilloma (CPP) and atypical choroid plexus papilloma (aCPP) have excellent outcomes. However, some CPP/aCPP relapse and may qualify for postoperative adjuvant treatment.

Methods: German patients from the International CPT-SIOP Registry diagnosed with CPP/aCPP between 2011 and 2023 were included and analysed according to initial staging (postoperative residual tumor [R+], metastases [M+]), biology, postoperative treatment strategy and outcome. Additionally, patients from the published CPT-SIOP-2000 trial (PMID34997889) were combined with the registry cohort for validation purpose.

Results: Ninety-three patients were identified (male: n = 53, female: n = 40). Median age at diagnosis was 1.9 (0.1–17.6) years. Initial staging was R0/M0 in n = 61, R+/M0 in n = 24, R0/M + in n = 5 and R+/M + in n = 3. aCPP was diagnosed in n = 38 patients. Molecular subgroup was available for n = 36: "adult" *n* = 3, "pediatric A" *n* = 21 and "pediatric B" *n* = 12 (6/12 aCPP). Median follow-up was 5.5 (± 0.99) years. Twelve tumors relapsed: R0/M0 *n* = 4, R+/M0 *n* = 7, R+/M + *n* = 1. One patient with relapse died. Most patients did not receive postoperative treatment (*n* = 88). Five patients (R0/M + *n* = 2; R+/M + *n* = 1; R0/M0 *n* = 2) received postoperative chemotherapy. None was irradiated during first-line treatment. In the enlarged cohort (*n* = 197), histological diagnosis had a significant impact on PFS (5y-PFS: CPP 90 ± 3.1, aCPP 78.6 ± 4.6, PFS = 0.01). Both, R+ (5y-PFS: R0 90.6 ± 2.6, *R* + 69.1 ± 7.0, PFS = 0.01) as well as molecular subgroup "pediatric B" (5y-PFS: pediatric A 95.2%±3.3%, pediatric B: 69.5 ± 8.6%, PFS = 0.02), were associated with inferior PFS, especially in aCPP.

Conclusion: Incomplete resection and biology impact on PFS especially in aCPP. These results extend the evidence for current stratification and treatment strategies.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- **Tumeur GLIONEURONALE**
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Review > Medicine (Baltimore). 2025 Mar 14;104(11):e41869.
doi: 10.1097/MD.0000000000041869.

Gamma knife radiosurgery for a rare Rosette-forming glioneuronal tumor in the brainstem region: A case report and literature review

Zhipeng Shen [1 2], Runzhu Ge [3 4], Dongxue Zhou [4], Yonglong Jin [5 6], Jie Wang [7], Shuyan Zhang [4], Chao Liu [4], Zishen Wang [7], Wei Wang [8], Yinuo Li [9], Weiwei Wang [4], Shosei Shimizu [4 9]

Affiliations + expand

PMID: 40101077 PMCID: PMC11922452 DOI: 10.1097/MD.0000000000041869

Abstract

Rationale: Rosette-forming glioneuronal tumor (RGNT) is a rare primary nervous system tumor, with limited treatment guidelines due to its rarity, especially in the brainstem. This report presents a unique case of brainstem RGNT treated with gamma knife radiosurgery (GKRS).

Patient concerns: A 35-year-old woman sought medical attention after sudden syncope and rapid decline in consciousness. Magnetic resonance imaging revealed a mass in the pineal region, extending to the brainstem and thalamus. Due to the critical location, only partial resection of the pineal tumor was possible, leaving most of the residual tumor in the vital brainstem area, requiring urgent intervention to control its growth and prevent sudden complications.

Diagnoses: Postoperative histopathological results confirmed a diagnosis of RGNT.

Interventions: The patient underwent 25 Gy/5 fractions of GKRS using the frameless Gamma Knife ICON™ (Elekta) device, as confirmed by cone-beam computed tomography scans for precise dose distribution and patient alignment.

Outcomes: GKRS was performed successfully and safely. The tumor significantly shrank 3 months post-GKRS, and the patient experienced symptom relief without any adverse effects.

Lessons: GKRS is considered an effective modality for RGNT in high-risk brainstem areas, minimizing risks while controlling tumor growth and alleviating symptoms. In addition, the frameless Gamma Knife ICON™ device enhanced patient comfort and treatment precision. GKRS offers a noninvasive alternative for similar RGNT cases.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- **Tumeur de REGION PINEALE**
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> Clin Cancer Res. 2025 Apr 14;31(8):1491-1503. doi: 10.1158/1078-0432.CCR-24-2785.

Germline Pathogenic DROSHA Variants Are Linked to Pineoblastoma and Wilms Tumor Predisposition

Peter N Fiorica [1], Lisa Golmard [2 3], Jung Kim [4], Riyue Bao [5 6], Frank Y Lin [7 8 9], Angshumoy Roy [7 8 9 10 11], Allison Pribnow [12], Melissa R Perrino [13], Julien Masliah-Planchon [2 3], Sophie Michalak-Provost [14], Jennifer Wong [2 3], Mathilde Filser [2 3], Dominique Stoppa-Lyonnet [2 15 16], Franck Bourdeaut [3 15 17], Afane Brahimi [18], Olivier Ingster [19], Giselle Saulnier Sholler [20], Sarah A Jackson [21], Mark M Sasaki [21], Trent Fowler [22 23], Anita Ng [24], Ryan J Corbett [25 26], Rebecca S Kaufman [27 28], Jeremy S Haley [29], David J Carey [29], Kuan-Lin Huang [30 31], Sharon J Diskin [27 28 32], Jo Lynne Rokita [25 26 33], Hussam Al-Kateb [34], Rose B McGee [13], Joshua D Schiffman [22 23 35], Kenneth S Chen [36 37], Douglas R Stewart [4], D Williams Parsons [7 8 9], Sharon E Plon [7 8 9], Kris Ann P Schultz [38], Kenan Onel [1 39 40]

Affiliations + expand

PMID: 39992227 PMCID: PMC11995001 DOI: 10.1158/1078-0432.CCR-24-2785

Abstract

Purpose: DROSHA, DGCR8, and DICER1 regulate miRNA biogenesis and are commonly mutated in cancer. Although DGCR8 and DICER1 germline pathogenic variants (GPV) cause autosomal dominant tumor predisposition, no association between DROSHA GPVs and clinical phenotypes has been reported.

Experimental design: After obtaining informed consent, sequencing was performed on germline and tumor samples from all patients. The occurrence of germline DROSHA GPVs was investigated in large pediatric and adult cancer datasets. The population prevalence of DROSHA GPVs was investigated in the UK Biobank and Geisinger DiscovEHR cohorts.

Results: We describe nine children from eight families with heterozygous DROSHA GPVs and a diagnosis of pineoblastoma (n = 8) or Wilms tumor (n = 1). A somatic second hit in DROSHA was detected in all eight tumors analyzed. All pineoblastoma tumors analyzed were classified as miRNA processing-altered 1 subtype. We estimate the population prevalence of germline DROSHA loss-of-function variants to be 1:3,875 to 1:4,843 but find no evidence for increased adult cancer risk.

Conclusions: This is the first report of DROSHA-related tumor predisposition. As pineoblastoma and Wilms tumor are also associated with DICER1 GPVs, our results suggest that the tissues of origin for these tumors are uniquely tolerant of general miRNA loss. The miRNA processing-altered 1 pineoblastoma subtype is associated with older age of diagnosis and better outcomes than other subtypes, suggesting DROSHA GPV status may have important clinical and prognostic significance. We suggest that genetic testing for DROSHA GPVs be considered for patients with pineoblastoma, Wilms tumor, or other DICER1-/DGCR8-related conditions and propose surveillance recommendations through research studies for individuals with DROSHA GPVs.

Multicenter Study > Eur J Surg Oncol. 2025 Aug;51(8):110058. doi: 10.1016/j.ejso.2025.110058. Epub 2025 Apr 22.

The establishment of machine learning prognostic prediction models for pineal region tumors based on SEER–A multicenter real–world study

Hao Wu [1], Aierpati Maimaiti [1], Jinlong Huang [2], Jing Xue [3], Qiang Fu [1], Zening Wang [1], Mamutijiang Muertizha [1], Yang Li [1], Di Li [1], Qingjiu Zhou [1], Yongxin Wang [4]

Affiliations + expand

PMID: 40300382 DOI: 10.1016/j.ejso.2025.110058

Abstract

Background: Pineal region tumors (PRT) are rare intracranial neoplasms with diverse pathological types and growth characteristics, leading to varied clinical manifestations. This study aims to develop machine learning (ML) models for survival prediction, offering valuable insights for medical practice in the management of PRTs.

Methods: Clinical information on PRTs was extracted from the Surveillance, Epidemiology, and End Results (SEER) database. The Kaplan-Meier (K-M) analysis was used to analyze the survival of PRT patients. Univariate and multivariate Cox regression analyses were conducted to identify risk factors for the survival of PRT patients. Then, nomograms were constructed. Seven ML models including Decision Tree, Logistic Regression, LightGBM, Random Forest, XGBoost, K-Nearest Neighbor Algorithm (KNN), and Support Vector Machine (SVM), were developed to predict the prognosis of PRT patients. The predictive value of ML models was evaluated by the area under the receiver's operating characteristic curve (AUC-ROC), tenfold cross verification, calibration curve, and decision curve analysis (DCA).

Results: Univariate and multivariate Cox regression revealed that age, histopathology, radiotherapy, and tumor size were independent risk factors for overall survival (OS). Histopathology, surgery, radiotherapy, and tumor size were risk factors for cancer-specific survival (CSS). K-M survival analysis revealed that age, histopathology, marital status, radiotherapy, sex, and surgery significantly impacted OS, while age, histopathology, marital status, race, radiotherapy, sex, and surgery significantly influenced CSS. In the prediction of OS, the ML models with the best clinical utility were RF, Logistic Regression, and XGBoost. For CSS, the most effective models were RF, LightGBM, and RF.

Conclusion: ML models demonstrate significant potential and high predictive efficacy in forecasting long-term postoperative survival in PRT patients, providing substantial clinical value.

Review > Brain Pathol. 2025 Jan;35(1):e13302. doi: 10.1111/bpa.13302. Epub 2024 Sep 1.

The 2022 WHO classification of tumors of the pituitary gland: An update on aggressive and metastatic pituitary neuroendocrine tumors

Olivera Casar-Borota [1] [2], Pia Burman [3], M Beatriz Lopes [4]

Affiliations + expand

PMID: 39218431 PMCID: PMC11669403 DOI: 10.1111/bpa.13302

Abstract

The vast majority of pituitary neuroendocrine tumors (PitNETs) are benign and slow growing with a low relapse rate over many years after surgical resection. However, about 40% are locally invasive and may not be surgically cured, and about one percentage demonstrate an aggressive clinical behavior. Exceptionally, these aggressive tumors may metastasize outside the sellar region to the central nervous system and/or systemically. The 2017 (4th Edition) WHO Classification of Pituitary Tumors abandoned the terminology "atypical adenoma" for tumors previously considered to have potential for a more aggressive behavior since its prognostic value was not established. The 2022 (5th Edition) WHO Classification of the Pituitary Tumors emphasizes the concept that morphological features distinguish indolent tumors from locally aggressive ones, however, the proposed histological subtypes are not consistent with the real life clinical characteristics of patients with aggressive tumors/carcinomas. So far, no single clinical, radiological or histological parameter can determine the risk of growth or malignant progression. Novel promising molecular prognostic markers, such as mutations in ATRX, TP53, SF3B1, and epigenetic DNA modifications, will need to be verified in larger tumor cohorts. In this review, we provide a critical analysis of the WHO guidelines for prognostic stratification and diagnosis of aggressive and metastatic PitNETs. In addition, we discuss the new WHO recommendations for changing ICD-O and ICD-11 codes for PitNET tumor behavior from a neoplasm either "benign" or "unspecified, borderline, or uncertain behavior" to "malignant" neoplasm regardless of the clinical presentation, histopathological subtype, and tumor location. We encourage multidisciplinary initiatives for integrated clinical, histological and molecular classification, which would enable early recognition of these challenging tumors and initiation of more appropriate and aggressive treatments, ultimately improving the outcome.

> Brain Tumor Res Treat. 2025 Apr;13(2):45-52. doi: 10.14791/btrt.2024.0045.

Treatment Outcomes and Prognostic Factors of Intracranial Germ Cell Tumors: A Single Institution Retrospective Study

Eunjong Lee [1], Kihwan Hwang [2], Kyeong-O Go [3], Jung Ho Han [2], Hyoung Soo Choi [4], Yu Jung Kim [5], Byung Se Choi [6], In Ah Kim [7], Gheeyoung Choe [8], Chae-Yong Kim [9]

Affiliations + expand

PMID: 40347126 PMCID: PMC12070076 DOI: 10.14791/btrt.2024.0045

Abstract

Background: This study analyzed the epidemiology and treatment outcomes of germ cell tumor patients at a single institution.

Methods: A retrospective analysis was conducted on intracranial germ cell tumor (iGCT) patients treated at a single tertiary hospital from 2004 to 2019. Patients were categorized based on treatment modality: Korean Society for Pediatric Neuro-Oncology (KSPNO) protocol or bleomycin, etoposide, and cisplatin with radiation therapy.

Results: Forty-nine iGCT patients treated with combined chemotherapy and radiotherapy were analyzed. The median age was 19 years (range: 6-40), with a median follow-up duration of 148.0 months (range: 10.5-265.5). Tumors were most common in the pineal gland (51.0%). Although no significant differences in outcomes were observed between treatment modalities, outcomes varied significantly by pathological type. The 10-year progression-free survival rates for germinoma and non-germinomatous germ cell tumors (NGGCTs) were 88.1% and 32.7%, respectively ($p=0.003$), while the 10-year overall survival rates were 92.9% and 67.5%, respectively ($p<0.001$). Fourteen patients experienced CTCAE (Common Terminology Criteria for Adverse Events) grade ≥3 adverse events, with one event-related death.

Conclusion: Pure germinoma demonstrated higher survival and lower recurrence rates compared to NGGCT. The KSPNO protocol appears to be an acceptable and safe treatment option for iGCT patients. Further multi-institutional studies with larger cohorts are warranted.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- **MEDULLOBLASTOME**
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> Neuro Oncol. 2025 Sep 17;27(8):2158-2169. doi: 10.1093/neuonc/noaf092.

Salvage therapies for first relapse of SHH medulloblastoma in early childhood

Craig Erker [1], Martin Mynarek [2 3], Marie Simbozel [4], Brandon T Craig [5], Virginia L Harrod [6], Andrea M Cappellano [7], Kenneth J Cohen [8], Vicente Santa-Maria Lopez [9], Andres Morales La Madrid [9], Chantel Cacciotti [10], Lorena Baroni [11], Ralph Salloum [12], Ashley S Margol [13], George Michaiel [14], Dolly Aguilera [15], Claire M Mazewski [15], Cassie N Kline [16], Jonathan L Finlay [17], Mohamed S Abdelbaki [18], Jeffrey C Murray [19], Kathleen Dorris [20], Bruce Crooks [1], Kevin F Ginn [21], Nisreen Amayiri [22], Stephan Tippelt [23], Gudrun Fleischhack [23], Svenja Tonn [3], Nicolas U Gerber [24], Alvaro Lassaletta [25], Jordan R Hansford [26 27], Sara Khan [12], Stephen W Gilheeney [28], Lindsey M Hoffman [29], Michal Zapotocky [30], Valérie Larouche [31], Shafqat Shah [32], Vijay Ramaswamy [33], Amar Gajjar [34], Sébastien Perreault [35], Sabine Mueller [36 37], Juliette Hukin [38], Sylvia Cheng [14], Zhihong J Wang [39], Kara Matheson [40], Simon Bailey [41], Eric Bouffet [33], Steven C Clifford [41], Giles Robinson [34], Christelle Dufour [4], Stefan Rutkowski [3], Lucie Lafay-Cousin [42]

Affiliations + expand

PMID: 40186336 PMCID: PMC12448823 DOI: 10.1093/neuonc/noaf092

Abstract

Background: Sonic hedgehog (SHH) medulloblastoma is the most common molecular group of infant and early childhood medulloblastoma (iMB) and has no standard of care at relapse. This work aimed to evaluate the post-relapse survival (PRS) and explore prognostic factors of patients with nodular desmoplastic (ND) and/or SHH iMB.

Methods: This international retrospective study included 147 subjects diagnosed with relapsed ND/SHH iMB between 1995 and 2017, <6 years old at original diagnosis, and treated without initial craniospinal irradiation (CSI). Univariable and multivariable Cox models with propensity score analyses were used to assess PRS for those in the curative intent cohort.

Results: The 3-year PRS was 61.6% (95% confidence interval [CI], 52.2-69.6). The median age at relapse was 3.4 years (interquartile range [IQR], 2.6-4.1). Those with local relapse (40.8%) more often received salvage treatment with surgery (P < .001), low-dose CSI (≤24 Gy; P < .001), or focal radiotherapy (P = .008). Patients not receiving CSI (40.5%) more often received salvage marrow-ablative chemotherapy (HDC + AuHCR [P < .001]). On multivariable analysis, CSI was associated with improved survival (hazard ratio [HR] 0.33 [95% CI, 0.13-0.86], P = .04). Salvage HDC + AuHCR, while clinically important, did not reach statistical significance (HR 0.24 [95% CI, 0.0054-1.025], P = .065).

Conclusions: Survival of patients with relapsed SHH iMB is not satisfactory and relies on treatments associated with toxicities including CSI and/or HDC + AuHCR. Cure at initial diagnosis to avoid relapse is crucial. For patients with localized relapse undergoing resection, alternative salvage regimens that avoid high-dose CSI (>24 Gy) can be considered.

> Ther Adv Med Oncol. 2025 Sep 20:17:17588359251344002. doi: 10.1177/17588359251344002. eCollection 2025.

Real-life experience with a "modified-MEMMAT" regimen for relapsed medulloblastoma

Antonella Cacchione [1], Giada Del Baldo [1 2], Federica D'Antonio [1 2], Valentina Di Ruscio [1], Giacomina Megaro [1], Chiara Pilotto [3], Assunta Tornesello [4], Alessandro Cocciolo [4], Sabina Vennarini [5], Silvia Chiesa [6], Andrea Carai [7], Andrea De Salvo [1], Giulia Albino [1], Giovanna Stefania Colafati [8], Irene Slavc [9], Angela Mastronuzzi [10]

Affiliations + expand

BEVACIZUMAB 14J TOPOTECAN IT 28 J FENOFIBRATE CELECOXIB ETOPOSIDE/CYCLOPHOSPHAMIDE /J

Abstract

Background: Medulloblastoma (MB) relapse is typically resistant to available treatments. An emerging alternative strategy focuses on disrupting tumor angiogenesis at various stages, using a combined metronomic anti-angiogenic approach.

Objectives: The study aims to assess the efficacy and safety of this modified treatment approach in managing recurrent MB in the pediatric population.

Designs: This study is a retrospective observational analysis involving 14 pediatric patients diagnosed with first or multiple recurrences of MB.

Methods: We analyzed clinical, molecular, radiological, and outcome data of our cohort treated using a modified Medulloblastoma European Multitarget Metronomic Anti-Angiogenic Trial (MEMMAT) strategy.

Results: Median age of patients was 11.6 years (range: 6.4-26 years). All 14 patients presented with a metastatic relapse after conventional treatments. The median time from primary diagnosis/prior relapse to the start of "modified MEMMAT" was 22 months (range: 2-60 months). Fifty-seven percent received the "modified MEMMAT" schema as second-line treatment, while 43% received it as third-line or beyond after recurrence. At a median follow-up of 17.9 months, the median overall survival (OS) from the MEMMAT start date was 18.2 months, and the median progression-free survival (PFS) was 12.8 months. OS at 12 and 24 months was 78.6% and 28.6%, respectively. PFS at 6 and 12 months was 100% and 55.0%, respectively. Treatment was globally well tolerated.

Conclusion: The modified MEMMAT strategy shows promise in treating recurrent MB, achieving a 12-month OS rate from date of starting treatment of 78.6%, with manageable toxicity. These findings suggest its potential as a viable option for heavily pre-treated pediatric patients, warranting further validation in larger prospective studies.

> J Neurooncol. 2025 Sep;174(2):401-409. doi: 10.1007/s11060-025-05070-5. Epub 2025 May 16.

Long-term neurocognitive sequelae in pediatric medulloblastoma survivors treated according to the HIT protocol

Iuliia A Aldeeva [1], Elena V Glebova [2 3], Roza A Sarkisyan [2], Elizaveta N Romanova [2], Nadezhda M Karpova [2], Valeriia G Shapovalova [2], Alexander F Karelin [3]

Affiliations + expand

PMID: 40377898 DOI: 10.1007/s11060-025-05070-5

Abstract

Objective: Medulloblastoma is the most prevalent malignant brain tumour in children. Although contemporary comprehensive anticancer therapy has been shown to result in favourable survival and relapse outcomes, the long-term toxic effects on cognitive and motor function remain a concern. This study aims to investigate the long-term neurotoxic effects on cognitive function in paediatric medulloblastoma survivors.

Method: Data from 70 patients (M_{age} = 12.7 ± 2.94 years, 40% female) in remission treated according to the HIT protocol who underwent comprehensive neuropsychological assessment were analyzed. General linear models (GLMs) were constructed to assess the contribution of remission duration, chemotherapy type, and radiation dose to variability in cognitive performance on the CANTAB and DTKI tests.

Results: GLM revealed that remission > 4 years was associated with poorer processing speed, attention, and executive functions: cognitive flexibility, inhibitory control, planning, and working memory compared to participants with shorter remission. Induction therapy with methotrexate had more pronounced long-term negative effects on processing speed. However, no significant effects were observed across different radiation doses.

Conclusions: Remission duration emerged as a more significant predictor of a poor neurocognitive outcome than chemotherapy type or radiation dose, that is, the longer the remission, the more pronounced the neurocognitive impairment becomes. This highlights the need for continued monitoring and the development of targeted rehabilitation interventions for paediatric medulloblastoma survivors.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- **MENINGIOME**
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> J Neurosurg Case Lessons. 2025 Mar 24;9(12):CASE24867. doi: 10.3171/CASE24867. Print 2025 Mar 24.

Preoperative PET/MRI and radio-guided surgery using [Cu64]DOTATATE in meningioma: a feasibility study. Illustrative case

Jana Ivanidze [1], Kate Rosen [2], Michael Zgaljardic [1], Jesse D Lawrence [2], Beth Ann Forader [3], Marcus Konner [1], Benjamin Liechty [4], Alexis Watson [1], Susan C Pannullo [2], Elizabeth Green [2], Jonathan P S Knisely [5], Nicolas A Karakatsanis [1], Sadek A Nehmeh [1], Theodore H Schwartz [2]

Affiliations + expand

PMID: 40127474 PMCID: PMC11933661 DOI: 10.3171/CASE24867

Abstract

Background: Meningiomas are the most common primary intracranial neoplasms. Gross-total resection, the primary treatment goal, is not achieved in up to 50% of patients, affecting progression-free and overall survival. The traditionally used intraoperative assessment of resection extent using the Simpson grade has recently been shown to be less accurate than postoperative MRI. Improving intraoperative resection extent delineation thus represents a paramount goal. Somatostatin receptor (SSTR)-targeted PET has improved meningioma management. [Cu64]DOTATATE is a clinically approved PET radiotracer that avidly binds to SSTR2 with properties similar to [Ga68]DOTATATE but with a significantly longer half-life of approximately 13 hours.

Observations: The authors assessed the feasibility of immediate preoperative [Cu64]DOTATATE PET/MRI and subsequent intraoperative tumor detection using a handheld gamma probe device typically used in sentinel node biopsy. They describe [Cu64]DOTATATE PET-guided surgical debulking of a meningioma and demonstrate the feasibility of intraoperative tumor detection using the gamma probe device, with activity 10 times higher than the background after exposing the tumor, decreasing by 50% after debulking. The authors further demonstrate 3-month clinical and PET/MRI outcomes, with accurate delineation of minimal residual viable tumor.

Lessons: This pilot study for the first time demonstrates the feasibility of preoperative PET with in vivo radio-guided surgery in meningiomas, laying the foundation for larger-scale prospective trials.

Meta-Analysis > Neurosurg Rev. 2025 Jan 6;48(1):23. doi: 10.1007/s10143-025-03180-2.

Efficacy, safety and dose patterns of tranexamic acid in meningioma surgery: a systematic review and updated meta-analysis of randomized controlled trials

Lucimário de Carvalho Barros [1], Clarissa Avancini [1], Paulo Eduardo Gonçalves [1], Wellingson Silva Paiva [2], Ricardo Queiroz Gurgel [1 3], Arthur Maynart Pereira Oliveira [4 5 6]

Affiliations + expand

PMID: 39760793 DOI: 10.1007/s10143-025-03180-2

Abstract

We reviewed the efficacy and safety of intravenous administration of tranexamic acid (TXA) in randomized trials involving patients undergoing intracranial meningioma resection surgery, with special emphasis on the effects of different dosages. A comprehensive search was conducted in the following databases: Cochrane, PubMed, Embase, Scopus, Lilacs, and Web of Science. Two reviewers independently screened titles and abstracts, reviewed the full texts and collected data. Efficacy outcomes analyzed included intraoperative blood loss, blood transfusion rate, duration of surgery, and length of hospital stay. The safety outcomes evaluated included postoperative complications such as seizures, thromboembolic events, and hematoma. A subgroup analysis was performed based on the dosage and timing of administration. Six randomized controlled trials (RCTs) were included, covering 881 patients. Meta-analysis of the data demonstrated that the use of TXA resulted in a significant reduction in intraoperative blood loss (Mean Difference [MD] = -270.26 ml, 95% CI [-422.84, -117.67], $p < 0.01$, $I^2 = 99\%$), blood transfusion rate (Relative Risk [RR] = 0.60, 95% CI: [0.46, 0.78], $p < 0.01$, $I^2 = 3\%$), duration of surgery (MD = -19.76 min, 95% CI: [-41.74, 2.23], $p < 0.01$, $I^2 = 75\%$), and length of hospital stay (MD: -0.48 days, 95% CI: [-0.93, -0.04], $p < 0.01$, $I^2 = 32\%$). No significant differences were found in the postoperative complications assessed. In the dosage analysis, the preoperative 20 mg/kg regimen, along with the intraoperative maintenance dose of 1 mg/kg/h, was more effective in reducing intraoperative blood loss in the TXA group, although not statistically significant (323.64 ml vs. 145.54 ml, $p = 0.29$). The administration of TXA in patients undergoing intracranial meningioma resection surgery showed beneficial results in all efficacy outcomes evaluated, without increasing postoperative complications. However, further studies, especially multicenter ones, are needed to confirm our results.

Multicenter Study > Lancet Oncol. 2025 Sep;26(9):1178-1190.
doi: 10.1016/S1470-2045(25)00422-X.

The effect of TERT promoter mutation on predicting meningioma outcomes: a multi-institutional cohort analysis

Karenna J Groff [1], Ruchit V Patel [2], Yang Feng [3], Hia S Ghosh [4], Miguel A Millares Chavez [5], Joseph O'Brien [5], William C Chen [6], Vijay Nitturi [7], Akshay V Save [8], Mark W Youngblood [9], Craig M Horbinski [9], James P Chandler [9], Felix Ehret [10], Chloe Gui [11], Justin Z Wang [11], Kristen Park [12], Sonia Ajmera [12], Marc Rosenblum [13], Abigail K Suwala [14], Catena Kresbach [15], Christopher W Mount [16], Ulrich Schüller [15], Sandro Santagata [17], Felix Sahm [14], Tejus A Bale [13], Christina Jackson [12], Timothy E Richardson [18], Chunyu Cai [19], Farshad Nassiri [11], Gelareh Zadeh [20], David Kaul [21], David Capper [22], Stephen T Magill [8], John G Golfinos [8], Chandra Sen [8], Akash J Patel [23], David R Raleigh [24], Jennifer Moliterno [25], Donato Pacione [8], Matija Snuderl [26], Wenya Linda Bi [27]

Affiliations + expand
PMID: 40907515 DOI: 10.1016/S1470-2045(25)00422-X

Abstract

Background: Molecular aberrations have been incorporated into tumour classification guidelines of meningioma. TERT-promoter (TERTp) mutation is associated with worse prognosis and is designated a WHO grade 3 biomarker. However, it remains unclear whether TERTp mutation is context-dependent, with other co-occurring genetic alterations potentially driving its association with prognosis. We sought to characterise the role of TERTp mutation in meningioma and guide TERTp sequencing.

Methods: We identified 1492 patients of all ages who had previously received surgery for meningioma across 14 medical centres in the USA, Canada, and Germany. Patients were eligible if they had post-surgical clinical or radiographical assessment of the resection site, and TERTp status evaluated by Nov 1, 2024. Multi-modal profiling was used to assess TERTp mutation, focal gene alterations-including CDKN2A/B loss-and copy number alterations. An adjusted WHO grade was calculated for TERTp-mutant meningiomas, incorporating all WHO criteria except TERTp status. Kaplan-Meier curves and multivariable Cox proportional hazards models were used to quantify the effect of TERTp mutation on the endpoints of overall survival and recurrence-free survival across adjusted WHO grade and co-occurring molecular alterations.

Findings: 64 (4·3%) of 1492 meningiomas were TERTp-mutant and 1428 (95·7%) were TERTp-wildtype. Of the TERTp-mutant meningiomas, 33 (51·6%) were from female patients and 31 (48·4%) were from male patients, and the overall median age was 67 years (IQR 60–75). Of the wildtype meningiomas, 965 (67·6%) were from female patients and 463 (32·4%) were from male patients, and the overall median age of the patients was 59 years (IQR 48–70). Data on race was inconsistently reported and thus excluded. The TERTp-mutant patients had a 5-year overall survival (49·4% [95% CI 33·7–72·4]) and 5-year recurrence-free survival (27·6% [95% CI 16·8–45·5]) resembling that of patients with WHO grade 3 TERTp-wildtype tumours (5-year overall survival 32·3% [95% CI 17·2–60·5], p=0·28, 5-year recurrence-free survival 14·3% [5·8–35·2], p=0·28). However, the TERTp-mutant group had heterogenous histological grading and was enriched for aggressive molecular features, with 1p loss present in 44 (77·2%) of 57 profiled tumours and CDKN2A/B loss in 24 (41·4%) of the 58 profiled tumours. Adjusting tumour grade revealed a subset of TERTp-mutant meningiomas that were more molecularly and clinically benign. Among TERTp-mutant tumours, CDKN2A/B loss played a defining role in stratifying tumour behaviour. Multivariable analysis confirmed this, with CDKN2A/B loss being significantly associated with shorter overall survival (HR 3·04 [95% CI 1·67–5·52], p=0·00026) and faster time to recurrence (HR 5·22 [95% CI 3·10–8·79], p<0·0001), while TERTp-mutation did not independently affect overall survival (HR 1·00 [95% CI 0·53–1·87], p=0·99) or recurrence-free survival (1·17 [95% CI 0·75–1·83], p=0·49). Sequencing for TERTp-mutation demonstrated clinical impact only among histologically WHO grade 2 meningiomas.

Interpretation: The indolent behaviour of certain TERTp-mutant meningiomas suggests that TERTp mutation is not sufficient to assign the most aggressive meningioma grade. Instead, TERT sequencing might offer prognostic utility in identifying high-risk cases among WHO grade 2 meningiomas.

Meta-Analysis > Acta Neurochir (Wien). 2025 Feb 5;167(1):35. doi: 10.1007/s00701-025-06436-4.

Gamma knife stereotactic radiosurgery for neurofibromatosis 2 (NF2)–associated meningiomas; a systematic review and meta–analysis

Mohammad Amin Habibi [1], Mohammad Sina Mirjani [2], Muhammad Hussain Ahmadvand [3], Pouria Delbari [3], Omid Alasti [4], Mohammad Taha Akbari Javar [5], Fatemeh Askari Yazdian [5], Romina Hamidi Rad [6], Ali Dinpazhouh [2], Mahdi Mehmandoost [7], Salem M Tos [8], Bardia Hajikarimloo [8], Amirmohammad Bahri [9], Fateme Aghaei [10], Mohammad Ali Abouei Mehrizi [11] [12]

Affiliations + expand

PMID: 39907804 PMCID: PMC11799078 DOI: 10.1007/s00701-025-06436-4

Abstract

Background: Neurofibromatosis type 2 (NF2)-related schwannomatosis is a rare genetic disorder associated with meningiomas. Stereotactic radiosurgery (SRS) has emerged as a potential non-invasive method. This study aims to synthesize the available evidence on using SRS to treat these tumors.

Methods: PubMed/Medline, Embase, Scopus, and Web of Science were searched until March 21, 2024. This study was prepared by adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

Results: Four studies were included comprising 101 patients with NF2-associated meningiomas treated with SRS. All included studies used gamma knife stereotactic radiosurgery (GKRS) as treatment modality. Overall survival rates remained high (100%) up to 3 years post-treatment, with slight declines at five years of 98% (95% CI: 0.95-1.01) and ten years of 68% (95% CI: 0.48-0.87). Progression-free survival rates were similarly favorable, with 95% (95% CI: 89-101%) at three years, 93% (95% CI: 86-99%) at five years, and 81% (95% CI: 51-111%) at ten years. The pooled radiation necrosis rate was 5% (95% CI: 3-7%), while the overall radiation toxicity rate was 16% (95% CI: 11-21%). Local tumor control rates were high at six months, and at 12 months, they were 100% (95% CI: 1.00-1.00).

Conclusion: GKRS demonstrates high efficacy and a favorable safety profile for NF2-associated meningiomas, offering a valuable treatment option for this challenging patient population.

> Neuro Oncol. 2025 Aug 16:noaf184. doi: 10.1093/neuonc/noaf184. Online ahead of print.

Multicenter basket trial for Central Nervous System tumors identifies activity of the CDK4/6 inhibitor abemaciclib in recurrent meningioma

Thomas J Kaley [1 2], Christian Grommes [1 3 2], Elizabeth Coffee [1], Robert J Young [4], Tara Morrison [5], Ahmad Daher [6], Lauren R Schaff [1 2], Yufei Deng [7], Subhiksha Nandakumar [7], Eli L Diamond [1 2], Lisa M DeAngelis [1 2], Katherine S Panageas [7], Igor Gavrilovic [1 2], Andrew Lin [1 2], Elena Pentsova [1 2], Jacqueline Stone [1 2], Bianca D Santomasso [1 2], Anna F Piotrowski [1 2], Suresh Nair [5], Nikolaus Schultz [7 3 8], Anne S Reiner [7], Ingo K Mellinghoff [1 3 2]

Affiliations + expand

PMID: 40842355 DOI: 10.1093/neuonc/noaf184

Abstract

Background: Central nervous system (CNS) tumors are associated with considerable morbidity and high mortality. Cyclin-dependent kinases (CDKs) regulate cell division in cancer, and CDK4/6 inhibitc are used for the treatment of breast cancer, representing an attractive therapy for different tumor types.

Methods: Here, we report mature results of a multicenter basket trial exploring the CDK4/6 inhibitor abemaciclib in patients with recurrent CNS tumors, including patients with glioma, primary CNS lymphoma, meningioma, and ependymoma. We expanded our cohort of meningioma patients base on preliminary evidence for activity. Patients were treated with 200mg oral abemaciclib twice daily fc days 1-28, following FDA recommendations for breast cancer. Primary outcomes included radiographic response rates and progression free survival (PFS) at 6 months post-treatment. We alsc evaluated overall survival (OS) and toxicity. Exploratory outcomes included next-generation sequencing of tumor biopsies.

Results: Most cohorts did not demonstrate activity with the exception of the cohort of patients with recurrent meningioma, including patients with grade 2 or 3 disease (19/22 meningioma patients). In that group, the median PFS was 15 months (95% CI: 6.5, not reached) and median OS was 32.9 months (95% CI: 10.7, not reached), the 6-month PFS was 68.2% (95% CI: 51.3%, 90.7%). All 22 patients were evaluable for radiographic response, showing stable disease in 16/22 (73%) and progressive disease in 6/22 patients (27%).

Conclusion: Our data suggests that abemaciclib improves PFS and OS in patients with advanced meningioma. The 6-month PFS with abemaciclib in this study (68.2%) exceeded RANO proposed benchmarks for activity (49%).Trial registration: NCT03220646.

> Neuro Oncol. 2025 Jun 28:noaf155. doi: 10.1093/neuonc/noaf155. Online ahead of print.

Mesothelin is a surface antigen present on human meningioma and can be effectively targeted by CAR T-cells

Rishab Ramapriyan [1], Fred G Barker 2nd [1], Leland G Richardson [1], Jing Sun [1], Gust Vandecandelaere [1], Jane M Shim [1], Guillaume De Vlaminck [1], Matthew Gaffey [1], Eric P Grewal [2], Masih Tazhibi [1], Kourosh Morshedy [3 4], Amir R Aref [3 5], Syeda M Batool [1], Xiaopeng Guo [1 6], Nazanin Ijad [3], Leonora Balaj [1], Hiroaki Wakimoto [1], Maria Martinez-Lage [7], Matthew J Frigault [7], Mark B Leick [1], Joshua D Bernstock [1], Wenya Linda Bi [1], Bob S Carter [1], E Antonio Chiocca [1], Jorg Dietrich [8], Elizabeth R Gerstner [8], Genevieve M Boland [5], Brian V Nahed [1], Scott R Plotkin [8], Russell W Jenkins [3 4 9], Priscilla K Brastianos [3 8], William T Curry [1], Marcela V Maus [2 7], Bryan D Choi [1]

Affiliations + expand

PMID: 40579924 DOI: 10.1093/neuonc/noaf155

Abstract

Background: Meningioma is the most common primary CNS tumor, with high-grade cases exhibiting aggressive behavior, frequent recurrence, and poor prognosis. Currently, no systemic therapies are approved for recurrent or malignant meningiomas. Chimeric antigen receptor (CAR) T-cell therapy has shown efficacy in hematologic malignancies and promise for solid tumors but its use for meningiomas has been underexplored. Mesothelin, a glycoprotein overexpressed in several solid tumors of mesodermal origin, may serve as a viable immunotherapeutic target. This study aimed to evaluate mesothelin as a CAR T-cell target in meningiomas.

Methods: Mesothelin expression was analyzed in patient-derived meningioma samples using immunohistochemistry, flow cytometry, and droplet digital PCR. Mesothelin-specific CAR T-cells were generated and evaluated in vitro, ex vivo using patient-derived organotypic tumor spheroids (PDOTS), and in vivo using orthotopic meningioma mouse models of human xenografts. Cytotoxicity, T-cell proliferation, cytokine secretion, and tumor clearance were assessed.

Results: Mesothelin was detected in a subset of tumors across all meningioma grades at the transcript and protein levels, with surface expression confirmed in patient-derived primary cells. Mesothelin-specific CAR T-cells exhibited potent and specific cytotoxicity, T-cell activation, and cytokine secretion in vitro and effectively eliminated PDOTS. In orthotopic human xenograft models, mesothelin CAR T-cell therapy led to significant tumor regression and prolonged survival.

Conclusions: Mesothelin is a viable CAR T-cell target for meningiomas, and mesothelin-specific CAR T-cell therapy shows strong preclinical efficacy. These findings provide a rationale for early-phase clinical trials of mesothelin CAR T-cell therapy in patients with refractory meningiomas.

Meta-Analysis > Neuro Oncol. 2025 Sep 8;27(7):1670-1685. doi: 10.1093/neuonc/noaf009.

Benchmarking the efficacy of salvage systemic therapies for recurrent meningioma: A RANO group systematic review and meta-analysis to guide clinical trial design

Rupesh Kotecha [1], Eyub Y Akdemir [2 1], Tugce Kutuk [1], Can Ilgın [3], Manmeet S Ahluwalia [4], Wenya L Bi [5], Jaishri Blakeley [6], Karan S Dixit [7], Ian F Dunn [8], Evanthia Galanis [9], Norbert Galldiks [10 11], Raymond Y Huang [12], Derek R Johnson [13], Thomas J Kaley [14], David O Kamson [15], Sylvia C Kurz [16], Michael W McDermott [17], Yazmin Odia [18], Matthias Preusser [19], Jeffrey Raizer [7], David A Reardon [20 21], C Leland Rogers [22], Roberta Ruda [23], David Schiff [24], Michael A Vogelbaum [25], Michael Weller [26], Patrick Y Wen [27], Minesh P Mehta [1]

Affiliations + expand

PMID: 39807850 PMCID: PMC12417825 (available on 2026-01-14) DOI: 10.1093/neuonc/noaf009

Abstract

Background: Despite advances in our understanding of the molecular underpinnings of meningioma progression and innovations in systemic and local treatments, recurrent meningiomas remain a substantial therapeutic challenge. The objective of this systematic review and meta-analysis is to provide a historical baseline, contemporary analysis, and propose a "rate of probable interest" to inform future clinical trial design and development on behalf of the Response Assessment in Neuro-Oncology meningioma group.

Methods: PubMed, ClinicalTrials.gov, and ASCOpubs databases were screened for clinical trials evaluating the activity of systemic therapies for adults with recurrent meningiomas. The pooled progression-free survival at 6-months and 1-year (PFS-6 and PFS-1 year) values were calculated using the random effects technique with I2 indices.

Results: The pooled PFS-6 and PFS-1 year rates for recurrent WHO grade 1 meningiomas were 43.6% (95% CI: 22.7-67.0%, I2 = 80%) and 21.7% (95% CI: 6.2-53.9%, I2 = 76%), and for grades 2-3 meningiomas, the PFS-6 was 38.0% (95% CI: 28.3-48.8%, I2 = 68%). In the targeted therapy group, PFS-6 and PFS-1 year rates stood at 62.0% (I2 = 58%) and 49.0% (I2 = 63%) for grade 1, while for grades 2-3 tumors, the PFS-6 rates with targeted therapy and immunotherapy were 42.1% (I^2 = 60%) and 46.0% (I^2 = 0%), respectively. The benchmarks were set at 67% and 54% for PFS-6 and PFS-1 year for grade 1 tumors, and PFS-6 of 49% for grades 2-3 tumors.

Conclusions: Several studies have reported outcomes in patients with recurrent meningiomas testing a variety of agents with modest, but variable and progressively increasing activity. In this context, we recommend new benchmarks for future trials to define efficacy of future investigational therapies.

Multicenter Study > Neuro Oncol. 2025 May 15;27(4):1004–1016. doi: 10.1093/neuonc/r

Validation and next–generation update of a DNA methylation–based recurrence predictor for meningioma: A multicenter prospective study

Alexander P Landry [1 2 3], Justin Z Wang [1 2 3], Vikas Patil [1 3], Chloe Gui [1 2 3], Yasin Mamatjan [1 3], Zeel Patel [4], Rebecca Yakubov [1 3], Ramneet Kaloti [1 3], Parnian Habibi [1 3], Mark Wilson [4], Andrew Ajisebutu [1 3], Yosef Ellenbogen [1 2 3], Qingxia Wei [1 3], Olivia Singh [1 3], Julio Sosa [1 3], Sheila Mansouri [1 3], Christopher Wilson [5], Aaron A Cohen-Gadol [6], Piiamaria Virtanen [7], Noah Burket [7], Matthew Blackwell [7], Jenna Koenig [7], Anthony Alfonso [7], Joseph Davis [7], Mohamed A Zaazoue [8 7], Ghazaleh Tabatabai [9 10 11], Marcos Tatagiba [12], Felix Behling [12], Jill S Barnholtz-Sloan [13 14], Andrew E Sloan [15], Silky Chotai [16], Lola B Chambless [16], Alireza Mansouri [17], Felix Ehret [18 19], David Capper [20 18], Derek S Tsang [21], Kenneth Aldape [22], Andrew Gao [23]; International Consortium on Meningiomas (ICOM); Farshad Nassiri [2 3], Gelareh Zadeh [2 3]

Affiliations + expand

PMID: 39503370 PMCID: PMC12083223 DOI: 10.1093/neuonc/noae236

Abstract

Background: We previously developed a DNA methylation-based risk predictor for meningioma, which has been used locally in a prospective fashion since its original publication. As a follow-up, we validate this model using a large prospective cohort and introduce a streamlined next-generation predictor compatible with newer methylation arrays.

Methods: Genome-wide methylation profiles were generated with the Illumina EPICArray. The performance of our next-generation predictor was compared with our original model and standard-of-care 2021 WHO grade using time-dependent receiver operating characteristic curves. An nomogram was generated by incorporating our methylation predictor with WHO grade and the extent of resection.

Results: A total of 1347 meningioma cases were utilized in the study, including 469 prospective cases from 3 institutions and an external cohort of 100 WHO grade 2 cases for model validation. Both the original and next-generation models significantly outperform the 2021 WHO grade in predicting early postoperative recurrence. Dichotomizing patients into grade-specific risk subgroups was predictive of outcomes within both WHO grades 1 and 2 tumors ($P < .05$), whereas all WHO grade 3 tumors were considered high-risk. Multivariable Cox regression demonstrated the benefit of adjuvant radiotherapy (RT) in high-risk cases specifically, reinforcing its informative role in clinical decision-making. Finally, our next-generation predictor contains nearly 10-fold fewer features than the original model, allowing for targeted arrays.

Conclusions: This next-generation DNA methylation-based meningioma outcome predictor significantly outperforms the 2021 WHO grading in predicting time to recurrence. We make this available as a point-and-click tool that will improve prognostication, inform patient selection for RT, and allow for molecularly stratified clinical trials.

> J Exp Clin Cancer Res. 2025 May 27;44(1):162. doi: 10.1186/s13046-025-03419-2.

Tumour–associated macrophage infiltration differs in meningioma genotypes, and is important in tumour dynamics

Ting Zhang [1 2], Claire L Adams [1], Gyorgy Fejer [3], Emanuela Ercolano [1], Jonathan Cutajar [4], Juri Na [1], Felix Sahm [5], C Oliver Hanemann [6]

Affiliations + expand

PMID: 40420192 PMCID: PMC12107748 DOI: 10.1186/s13046-025-03419-2

Abstract

Background: Meningiomas are the most common primary intracranial tumours, with clinical behaviours ranging from benign to highly aggressive forms. The World Health Organisation classifies meningiomas into various grades, guiding prognosis and treatment. While surgery is effective for low-grade meningiomas, certain grade 1 tumours, as well as grade 2, 3, and recurrent cases are more aggressive and require new therapeutic approaches. Immunotherapy shows promise, with early-stage clinical trials demonstrating encouraging results. The tumour microenvironment (TME), particularly tumour-associated macrophages (TAMs), plays a pivotal role in tumour progression. TAMs influence tumour growth, metastasis, and immune evasion. However, their role in meningiomas, especially in relation to genomic mutations, remains poorly understood. Understanding how genetic alterations affect the TME is critical for developing targeted immunotherapies.

Methods: This study employed multiplex immunohistochemistry and bulk RNA sequencing to explore immune infiltration in genetically stratified meningioma tissues and matched three-dimensional (3D) spheroid models. We compared immune cell populations across parental tissues, two-dimensional (2D) monolayer cultures, and 3D spheroid models. In addition, co-culture experiments were conducted, introducing M2-polarised macrophages derived from peripheral blood mononuclear cells to study the interactions between immune cells and tumour cells.

Results: Our findings revealed significant differences in the immune infiltration patterns associated with specific genotypes and methylation classes, especially M2-like TAMs. Notably, the 3D spheroid models more closely replicated the TME observed in parental tissues compared to traditional 2D monolayer cultures, offering a superior platform for immune infiltration studies. Furthermore, co-culture experiments demonstrated that M2-polarised macrophages could effectively infiltrate tumour cells, promote tumour cell proliferation while inhibiting invasion, suggesting IL-6-mediated signalling in tumour progression.

Conclusions: These findings suggest that 3D co-culture models offer an excellent system for studying the role of immune cells, specifically TAMs, in meningioma progression. By providing a more accurate representation of the TME, these models can help identify novel immunotherapy strategies aimed at modulating the immune response within meningiomas. Ultimately, this approach may improve therapeutic outcomes and quality of life for patients with meningioma by enhancing the effectiveness of existing treatments or by offering new immunotherapeutic options.

> J Nucl Med. 2025 Aug 7:jnumed.125.269633. doi: 10.2967/jnumed.125.269633.
Online ahead of print.

[^{177}Lu]Lu-DOTATATE for Recurrent Meningioma (LUMEN-1, EORTC-2334-BTG): Study Protocol for a Randomized Phase II Trial

Nathalie L Albert [1], Emeline Tabouret [2 3], Emilie Le Rhun [4], Felix Sahm [5], Julia Furtner [6], Joerg-Christian Tonn [7], Christian Alfano [8], José Pais Silva [8], Anne-Sophie Govaerts [8], Thierry Gorlia [8], Osvaldo Mirante [9], Giuseppe Minniti [10], Michael Weller [11], Matthias Preusser; European Organisation for Research and Treatment of Cancer Brain Tumor Group

Affiliations + expand

Essai LUMEN-1 au CEM et Essai E-LUMEN à Brest

Abstract

There are no established treatment options for patients with meningioma recurring after surgery and radiotherapy. Somatostatin receptor type 2 (SSTR2) is highly expressed in meningiomas, and SSTR2-targeting radionuclide therapy with [^{177}Lu]Lu-DOTATATE has shown potential activity in the treatment of meningioma in uncontrolled and small studies. **Methods:** EORTC-2334-BTG (LUMEN-1, NCT06326190) is a randomized, multicenter, phase II trial in patients with recurrent World Health Organization (WHO) grade 1, 2, or 3 meningioma. In total, 136 patients will be randomized in a 2:1 ratio to [^{177}Lu]Lu-DOTATATE (≤4 doses of 7.4 GBq given every 4 wk) or local standard of care (hydroxyurea, bevacizumab, sunitinib, octreotide, everolimus, or observation). The main eligibility criteria include age 18 y or older; neuropathologically confirmed meningioma of WHO grade 1, 2, or 3; WHO performance score of 0-2; measurable disease on MRI (≥10 × 10 mm); radiologically documented progression of any existing tumor (growth > 25% or new lesions) or appearance of new lesions within the last 2 y; SSTR positivity by PET imaging (SUV_{max} > 2.3); at least 1 prior surgery and at least 1 line of radiotherapy; and no prior systemic therapy. The primary efficacy endpoint is locally assessed progression-free survival according to Response Assessment in Neuro-Oncology MRI meningioma criteria, and secondary endpoints include radiologic response rate, overall survival, safety, health-related quality of life, and neurologic function. The trial protocol includes a comprehensive exploratory translational research program with dosimetry and imaging-based and tissue-based investigations. LUMEN-1 was activated in March 2025 and will enroll patients in 35 sites in 10 countries across Europe, with primary endpoint collection planned after 2 y and study completion after 5 y. To our knowledge, EORTC-2334-BTG (LUMEN-1, NCT06326190) is the first prospective randomized trial investigating the efficacy of [^{177}Lu]Lu-DOTATATE in patients with recurrent meningioma.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- **HEMANGIOPERICYTOME**
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

Meta-Analysis > Sci Rep. 2025 Jul 2;15(1):23368. doi: 10.1038/s41598-025-02170-0.

A systematic review and meta-analysis on the efficacy of postoperative radiotherapy after gross total resection of intracranial solitary fibrous tumors

Min Kyun Na [# 1], Kyu-Sun Choi [# 1], Tae Ho Lim [2], Hyungoo Shin [2], Juncheol Lee [2], Heekyung Lee [2], Wonhee Kim [3], Jae Guk Kim [3], Youngsuk Cho [4], Chiwon Ahn [5], Jae Hwan Kim [5], Bo-Hyoung Jang [6], Myeong Namgung [7], Sae Min Kwon [8]

Affiliations + expand

PMID: 40603922 PMCID: PMC12222894 DOI: 10.1038/s41598-025-02170-0

Abstract

The efficacy of postoperative radiotherapy (PORT) after gross total resection (GTR) for intracranial solitary fibrous tumors (SFT) remains unclear due to the inconsistent results of previous studies, with some studies suggesting improved outcomes in progression-free survival (PFS) and overall survival (OS), while others report no significant benefit. Therefore, by evaluating and synthesizing data from relevant studies, we aimed to investigate the role of PORT, as compared with surgery alone, in survival outcomes after GTR of intracranial SFT. A systematic literature search, adhering to PRISMA guidelines and using Medline, Embase, and the Cochrane Library to identify relevant literature. The outcomes of interest included progression-free survival (PFS), overall survival (OS), and metastasis-free survival (MFS) at 3, 5, and 10 years, respectively. Differences between the two cohorts (GTR + PORT vs. GTR only) were estimated by calculating the hazard ratios. Twelve studies, including data from 419 patients (GTR + PORT, n = 225 vs. GTR, n = 194), were selected for meta-analysis. Pooled hazard ratios revealed that the PORT cohort showed sustained superiority in both PFS and OS compared with the surgery-only cohort after GTR of the tumor. These results were consistent with those of a subgroup analysis that focused on grade 2 and 3 intracranial SFT. However, no significant improvement was observed in MFS with PORT addition. This study underscores the importance of PORT in enhancing the PFS and OS of patients with intracranial SFT after GTR. These findings suggest that PORT should be considered an effective treatment strategy for all patients with intracranial SFT, irrespective of the extent of resection.

Meta-Analysis > J Clin Neurosci. 2025 Jul:137:111302. doi: 10.1016/j.jocn.2025.111302. Epub 2025 May 7.

Postoperative stereotactic radiosurgery for intracranial solitary fibrous tumors/hemangiopericytomas: A systematic review and meta-analysis

Bardia Hajikarimloo [1], Salem M Tos [2], Ibrahim Mohammadzadeh [3], Mohammad Amin Habibi [4]

Affiliations + expand

PMID: 40339242 DOI: 10.1016/j.jocn.2025.111302

Abstract

Background: Intracranial solitary fibrous tumors (SFTs) and hemangiopericytomas (HPCs) are infrequent neoplastic lesions characterized by hypercellularity and considerable vascularization. SFT/HPCs are associated with a considerably higher likelihood of recurrence and development of metastasis. Maximal safe resection with the goal of achieving gross total resection (GTR) is the gold-standard therapeutic option; however, it is challenging due to considerable vascularization and susceptibility to intraoperative hemorrhage concurrent with adjacency to the critical neurovascular structures. SRS has been demonstrated as an efficient adjuvant treatment option for intracranial SFT/HPCs. This meta-analysis evaluated the efficacy and safety of postoperative SRS in intracranial SFT/HPCs.

Methods: On February 5, 2025, a comprehensive search of PubMed, Embase, Scopus, and Web of Science was conducted. Studies that evaluated SRS in intracranial SFT/HPCs and reported local tumor control (LTC), overall survival (OS), and progression-free survival (PFS) were included. The analysis was conducted in the R program.

Results: Ten studies with 228 patients and 469 SFT/HPCs were included. The meta-analysis showed a pooled overall LTC rate of 68 % (95 %CI: 55 %-80 %), 1-year LTC rate of 94 % (95 %CI: 90 %-97 %), and 5-year LTC rate of 60 % (95 %CI: 42 %-76 %). The meta-analysis revealed a pooled overall OS rate of 59 % (95 %CI: 43 %-75 %), 5-year OS rate of 85 % (95 %CI: 67 %-97 %), and 10-year OS rate of 64 % (95 %CI: 25 %-95 %). In addition, The meta-analysis revealed a pooled ARE rate of 6 % (95 %CI: 3 %-9 %).

Conclusion: Postoperative SRS is an efficient and safe adjuvant therapeutic option for intracranial SFT/HPCs. SRS has comparative results to conventional RT with lower ARE. Further prospective multicenter studies with large sample sizes are required to validate our findings.

Review > Neurol Res. 2025 Aug 28:1-14. doi: 10.1080/01616412.2025.2553861.
Online ahead of print.

Stereotactic radiosurgery in the management of intracranial hemangiopericytomas: a meta-analytic review

João Vitor Andrade Fernandes [1], Maria Antonia Oliveira Machado Pereira [2], Ocílio Ribeiro Gonçalves [3], Paweł Łajczak [4], Rafael Reis de Oliveira [5], Luana Miyahira Makita [6], Maurus Marques de Almeida Holanda [1]

Affiliations + expand
PMID: 40877197 DOI: 10.1080/01616412.2025.2553861

Abstract

Introduction: Intracranial hemangiopericytomas (HPCs) are rare and aggressive mesenchymal tumors with high rates of local recurrence and metastasis. This meta-analysis evaluates the effectiveness of stereotactic radiosurgery (SRS) in managing these tumors.

Methods: A systematic search was conducted up to January 2025 for studies reporting outcomes of SRS in intracranial HPCs. Inclusion criteria comprised original studies with extractable data on at least one predefined outcome. Data were synthesized using random-effects meta-analysis, with heterogeneity assessed by I^2 statistics. Sensitivity analyses and influence diagnostics were performed. Risk of bias was evaluated using ROBINS-I, and publication bias was assessed with funnel plots and Egger's test when applicable.

Results: Sixteen studies (329 patients, 483 tumors) were included. Tumor size reduction occurred in 47.9% (95% CI: 36.1-59.7%; I^2 = 81%) and complete response in 29.9% (95% CI: 16.5-43.3%; I^2 = 74%). Tumor progression was reported in 22.7% (95% CI: 9.1-36.4%; I^2 = 90%) and tumor stability in 12.1% (95% CI: 6.2-17.9%; I^2 = 63%). Extracranial metastases occurred in 21.3% of patients (95% CI: 16.1-26.5%; I^2 = 0%). Neurological improvement was observed in 16.0% (95% CI: 9.2-22.8%; I^2 = 28%), and mortality reached 31.3% (95% CI: 20.7-41.8%; I^2 = 71%). Treatment-related complications occurred in 10.8% (95% CI: 2.5-19.2%; I^2 = 0%). No major publication bias was identified.

Conclusion: SRS provides meaningful tumor control and favorable safety in intracranial HPCs, with notable rates of size reduction and complete response, though progression, metastasis, and mortality remain substantial.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- **ADENOME HYPOPHYSAIRE**
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

> Neurosurgery. 2025 Mar 1;96(3):611-621. doi: 10.1227/neu.0000000000003142. Epub 2024 Aug 22.

Treatment Strategies and Long-Term Outcomes in Silent Corticotroph Adenomas: A Single-Center Retrospective Study of 367 Cases

Wenqiang He [1 2 3 4 5], Shun Yao [1 2 3 4 5], Yifei Yu [5 6], Zhengyuan Chen [1 2 3 4 5], Qilin Zhang [1 2 3 4 5], Nidan Qiao [1 2 3 4 5], Ming Shen [1 2 3 4 5], Xuefei Shou [1 2 3 4 5], Zengyi Ma [1 2 3 4 5], Yongfei Wang [1 2 3 4 5]

Affiliations + expand

PMID: 39171920 DOI: 10.1227/neu.0000000000003142

Abstract

Background and objectives: Silent corticotroph adenoma (SCA) is a high-risk pituitary neuroendocrine tumor (PitNET) which exhibits more aggressive behavior than other nonfunctioning PitNETs. Some SCAs are observed to recur after total resection (TR). We aim to discuss the long-term outcomes after endoscopic endonasal surgery for SCAs and explore optimal treatment after operation.

Methods: Clinical data and intraoperative videos from 367 SCAs who underwent endoscopic endonasal surgery were retrospectively collected. Patients were categorized into TR and subtotal resection (STR) groups according to 3-month postoperative MRIs. Based on close-up intraoperative observation of the relationship between tumor and pituitary gland, diaphragm, and medial wall cavernous sinus, patients in the TR group were further subdivided into gross total resection (GTR) and near total resection (NTR) groups. Patients in the STR group were subdivided as STR followed by observation (STR + ob) and STR followed by adjuvant stereotactic radiosurgery (SRS) (STR + SRS). Kaplan-Meier analysis was used to compare the event-free survival among these subgroups.

Results: Headache (27.5%) and vision loss (55.3%) were the most common presenting symptoms. Cavernous sinus (CS) invasion was confirmed intraoperatively in 167 (45.5%) patients. After operation, 175 (47.7%), 83 (22.6%), 32 (8.7%), and 77 (21%) patients were divided into GTR, NTR, STR + ob, and STR + SRS groups, respectively. The mean follow-up time was 40.9 ± 25.8 months. There were 0, 17 (20.5%), 9 (28.1%), and 4 (5.2%) patients noted to have PitNET recurrence or progression in GTR, NTR, STR + ob, and STR + SRS groups, respectively. Event-free survival distribution in the NTR group was similar to that in the STR + ob group (P = .696), which was significantly lower than that in the STR + SRS group (P = .008). Adrenocorticotropic hormone (ACTH)-negative SCAs have lower preoperative ACTH levels and were more likely to invade CS than ACTH-positive SCAs.

Conclusion: CS invasion was commonly seen in SCAs, often precluding GTR. Radical surgery and close follow-up were proposed. Early postoperative adjuvant SRS for remnant tumor should be considered.

> Front Oncol. 2025 Feb 4:15:1519445. doi: 10.3389/fonc.2025.1519445. eCollection 2025.

Fractionated robotic radiosurgery for unfavorable nonfunctioning pituitary macroadenoma: 5-year outcomes from a single institution protocol

Akrita Bhatnagar [1], Monica Pernia Marin [2], Jonathan W Lischalk [3], Min Ji Koh [1], Siviero Agazzi [4], Simeng Suy [1], Brent T Harris [5], Susmeeta T Sharma [6], Edward Aulisi [7], Amjad Anaizi [8], Mohamed H Khattab [9], Walter C Jean [# 4 10], Sean P Collins [# 9], Brian T Collins [# 9]

Affiliations + expand

PMID: 39968072 PMCID: PMC11832394 DOI: 10.3389/fonc.2025.1519445

Abstract

Objective: Nonfunctioning macroadenoma is a commonly diagnosed pituitary tumor. Resection is the favored treatment, with radiosurgery often utilized for residual or progressing disease. Long-term outcomes are established in the literature for single-fraction frame-based radiosurgery, but mature outcomes are lacking for fractionated frameless radiosurgery. We report our institution's 5-year efficacy and toxicity results for unfavorable nonfunctioning pituitary macroadenoma patients treated with 5-fraction robotic radiosurgery.

Methods: Between 2010 and 2020, patients who completed 5-fraction robotic radiosurgery for the treatment of unfavorable nonfunctioning pituitary macroadenomas were included. A tumor was considered unfavorable if the gross tumor volume (GTV) was larger than 5 cc or if it closely approached a critical structure (optic apparatus, brainstem, or pituitary gland). Local control was calculated using the Kaplan-Meier method.

Results: Twenty predominantly female patients (60%), ages 21-77 (median: 53 years), were included in this study. All underwent primary resection at the time of diagnosis. The indication for radiosurgery was tumor progression (n = 14, 70%) or residual tumor after subtotal resection (n = 6, 30%). Eighty-five percent of patients treated with radiosurgery (n = 17) had cavernous sinus involvement. Median GTV was 3.4 cm^3 (range: 0.3-20.8 cm^3), and 40% of the tumors had suprasellar extension. A mean dose of 28.8 Gy (range: 25-30 Gy) was delivered to a median isodose line of 80% (range: 75%-89%). The median optic chiasm maximum point dose was 21.8 Gy (range: 12.0-25.0 Gy). Acute toxicity was minimal with eight patients (40%) developing short-lived headaches and one patient (5%) developing a brief ipsilateral sixth nerve palsy. There was no late radiation-induced neurologic or optic dysfunction identified in this cohort. At a median follow-up of 5 years, local control was 94%. There was one in-field failure pathologically confirmed following surgery for pituitary hemorrhage and two radiographically confirmed out-of-field failures in patients with larger tumors (>20 cc).

Conclusions: The treatment of unfavorable nonfunctioning pituitary macroadenoma with 5-fraction robotic radiosurgery provides excellent local control to date, with acceptable toxicity. However, tumors with GTVs greater than 20 cc may still require conventionally fractionated treatment with a margin to optimize local control.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- **METASTASES CEREBRALES**
- SCHWANNOME VESTIBULAIRE

Clinical Trial > Med. 2025 Jan 10;6(1):100513. doi: 10.1016/j.medj.2024.09.002. Epub 2024 Oct 9.

First-line zorifertinib for EGFR-mutant non-small cell lung cancer with central nervous system metastases: The phase 3 EVEREST trial

Qing Zhou [1], Yan Yu [2], Ligang Xing [3], Ying Cheng [4], Ying Wang [5], Yueyin Pan [6], Yun Fan [7], Jianhua Shi [8], Guojun Zhang [9], Jiuwei Cui [10], Jianying Zhou [11], Yong Song [12], Wu Zhuang [13], Zhiyong Ma [14], Yanping Hu [15], Gaofeng Li [16], Xiaorong Dong [17], Jifeng Feng [18], Shun Lu [19], Jingxun Wu [20], Juan Li [21], Longzhen Zhang [22], Dong Wang [23], Xinhua Xu [24], Tsung-Ying Yang [25], Nong Yang [26], Yubiao Guo [27], Jun Zhao [28], Yu Yao [29], Diansheng Zhong [30], Bing Xia [31], Cheng-Ta Yang [32], Bo Zhu [33], Ping Sun [34], Byoung Yong Shim [35], Yuan Chen [36], Zhen Wang [37], Myung-Ju Ahn [38], Jie Wang [39], Yi-Long Wu [40]

Affiliations + expand

PMID: 39389055 DOI: 10.1016/j.medj.2024.09.002

Abstract

Background: Zorifertinib (AZD3759), an epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) with high blood-brain barrier penetration capability, demonstrated promising intracranial and systemic antitumor activity in phase 1 and 2 studies in central nervous system (CNS)-metastatic patients.

Methods: In this phase 3 EVEREST trial (ClinicalTrials.gov: NCT03653546), patients with EGFR-sensitizing mutations, advanced treatment-naive non-small cell lung cancer (NSCLC), and non-irradiated symptomatic or asymptomatic CNS metastases were randomized (1:1) to zorifertinib or first-generation EGFR-TKI (gefitinib or erlotinib; control). The primary endpoint was blinded independent central review (BICR)-assessed progression-free survival (PFS) per RECIST1.1.

Findings: Overall, 439 patients were randomized (zorifertinib n = 220; control n = 219). Most patients had the EGFR L858R mutation (55%) or >3 CNS lesions (54%). Median PFS was significantly longer with zorifertinib versus control (9.6 versus 6.9 months; hazard ratio [HR], 0.719; 95% confidence interval [CI], 0.580-0.893; p = 0.0024). Zorifertinib significantly prolonged intracranial PFS versus control (BICR per modified RECIST1.1: HR, 0.467; 95% CI, 0.352-0.619; investigator per RANO-BM: HR, 0.627; 95% CI, 0.466-0.844). Overall survival (OS) was immature; the estimated median OS was 37.3 months with zorifertinib and 31.8 months with control (HR, 0.833; 95% CI, 0.524-1.283) in patients subsequently treated with third-generation EGFR-TKIs. Safety profiles were consistent with previously reported data for zorifertinib.

Conclusions: Zorifertinib significantly improved systemic and intracranial PFS versus first-generation EGFR-TKIs; adverse events were manageable. Sequential use of zorifertinib and third-generation EGFR-TKIs showed the potential to prolong patients' survival. The results favor zorifertinib as a novel, well-validated first-line option for CNS-metastatic patients with EGFR-mutant NSCLC.

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2025**
- **Publications de 2025**
- GLIOBLASTOME et Gliome de haut grade
- GLIOME DE BAS GRADE
- GLIOME DE LA LIGNE MEDIANE et du TRONC
- ASTROBLASTOME
- XANTHOASTROCYTOME
- EPENDYMOME
- Tumeur des PLEXUS CHOROIDES
- Tumeur GLIONEURONALE
- Tumeur de REGION PINEALE
- MEDULLOBLASTOME
- MENINGIOME
- HEMANGIOPERICYTOME
- ADENOME HYPOPHYSAIRE
- METASTASES CEREBRALES
- **SCHWANNOME VESTIBULAIRE**

Meta-Analysis > World Neurosurg. 2025 May:197:123938. doi: 10.1016/j.wneu.2025.123938. Epub 2025 Mar 22.

Incidence and Risk Factors of Delayed Facial Paralysis After Vestibular Schwannoma Resection: A Systematic Review and Meta-Analysis

Xiezhuo Zhang [1], Hongbo Wen [1], Guohuan Chen [2]

Affiliations + expand

PMID: 40127861 DOI: 10.1016/j.wneu.2025.123938

Free article

Abstract

Objective: Delayed facial nerve paralysis (DFNP) is a common complication after vestibular schwannoma surgery. Previous studies have focused on immediate facial nerve paralysis, and the risk factors for developing DFNP remain largely unclear. This study aimed to determine the incidence and risk factors of DFNP in patients after vestibular schwannoma resection.

Methods: Up to 8 October 2024, PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wanfang Data, and China Science and Technology Journal Database were searched to extract the related data of DFNP. The pooled incidence of DFNP was calculated. Possible risk factors of DFNP were conducted to report the odds ratio/weighted mean difference (WMD), and their 95% confidence intervals (CIs).

Results: Twenty-seven studies were included, and 8656 patients underwent vestibular schwannoma resection. The incidence of DFNP in patients with vestibular schwannoma who underwent microsurgical resection was 12.3% (95% CI: 9.4%, 15.1%). The results of the influencing factor analysis showed that age (WMD: -4.28, 95% CI: -5.66, -2.91) and tumor size (WMD: 0.17, 95% CI: 0.01, 0.22) were related to the incidence of DFNP in patients after vestibular schwannoma resection.

Conclusions: DFNP is a complication after vestibular schwannoma surgery that cannot be ignored. The risk factors (age and tumor size) of DFNP in patients after vestibular schwannoma surgery still need to be considered, and clinical management of high-risk groups should be strengthened in clinical practice.

Meta-Analysis > Neurosurg Rev. 2025 Feb 10;48(1):229. doi: 10.1007/s10143-025-03237-2.

Evaluating the effectiveness and complications of the Retrosigmoid, Translabyrinthine and Middle Fossa approaches in vestibular Schwannoma surgical management: a comprehensive systematic review and meta-analysis of 6,889 patients

Fabricio Garcia-Torrico [1], Cristian D Mendieta [2], Fernando De Nigris Vasconcellos [3], Vanessa Pamela Salolin Vargas [4], Marcos Scalise [5], Kevin Mamani-Julian [6], Marcos Antônio Dias Vilela [7], Emanuela Binello [3], Carolina Benjamin [8]

Affiliations + expand

PMID: 39930308 DOI: 10.1007/s10143-025-03237-2

Abstract

Surgical resection stands as one of the potential therapeutic methods for vestibular schwannomas (VS). However, in the management of patients with VS, there is limited literature directly comparing the Retrosigmoid approach (RSA) with the Translabyrinthine Approach (TLA) and Middle Fossa Approach (MFA). This gap arises because the MFA is typically reserved for smaller intracanalicular tumors, while the RSA and TLA are preferred for larger lesions. Our objective was to assess and compare the outcomes and safety profile of these three different surgical approaches. A comprehensive search was performed on PubMed, Embase, and Cochrane Library for studies comparing RSA with TLA and MFA in patients with VS. The main outcomes of interest were hearing preservation, facial nerve function, extent of resection, and postoperative complications. Statistical analyses were performed using Review Manager. The I^2 test was employed for heterogeneity assessment, while the risk of bias was evaluated utilizing ROBINS-I. We included 6,889 patients from 32 observational studies. RSA was used to manage VS in 3,352 (48,7%) patients. Our comparative hearing preservation analysis revealed no significant difference in patient improvement between RSA and MFA, with a risk ratio (RR) of 1.18 (95% CI: 0.76-1.85, p = 0.46, I^2:0%). Late facial nerve preservation comparing RSA and TLA showed RR = 0.91(95% CI: 0.77-1.07, p = 0.25, I^2:32%), while RSA with MFA a RR = 0.98 (95% CI: 0.92-1.04, p = 0.53, I^2:87%). The cerebrospinal fluid (CSF) leak showed no significant difference in risk RR = 1.18 (95% CI: 0.92-1.51, p = 0.21; I^2:0%) and RR = 1.14 (95% CI: 0.70-1.83; p = 0.60, I^2:26%) comparing RSA with TLA and MFA respectively. The evidence synthesized in this meta-analysis suggests equivalent hearing preservation and facial nerve function in managing VS patients across the different RSA and MFA surgical approaches analyzed. However, in comparison to TLA and MFA, RSA stood out exhibiting fewer occurrences of postoperative complications consisting of hydrocephalus, and CSF leaks.

Meta-Analysis > Otolaryngol Head Neck Surg. 2025 Mar;172(3):774-786. doi: 10.1002/ohn.1031. Epub 2024 Oct 22.

Translabyrinthine versus Retrosigmoid Approach for Vestibular Schwannoma: A Systematic Review and An Updated Meta-Analysis

Frederico L Gibbon [1 2], Rafaela J Lindner [3], Antônio D M Vial [1], Guilherme G da Silva [1], Lucca B Palavani [4], Gabriel Semione [5], Paulo V Worm [1], Gustavo R Isolan [6], Vagner A R da Silva [7], Ricardo F Bento [8], Rick A Friedman [9], Joel Lavinsky [2]

Affiliations + expand

PMID: 39435621 DOI: 10.1002/ohn.1031

Abstract

Objective: Several approaches can be used in the surgical treatment of vestibular schwannoma (VS), and the best approach remains uncertain in the literature. This systematic review and meta-analysis aim to compare the translabyrinthine approach (TLA) with the retrosigmoid approach (RSA) for VS in terms of postoperative complications.

Data sources: PubMed, Web of Science, Embase, and Cochrane.

Review methods: The primary outcome was cerebrospinal fluid (CSF) leak; secondary outcomes were facial nerve dysfunction (FND), length of stay (LOS), and meningitis. Statistical analysis was performed using RStudio 2024.04.1 + 748. Heterogeneity was assessed with I^2 statistics. We performed sensitivity analysis with subgroup analysis and meta-regression. Risk of bias was assessed using ROBINS-I.

Results: Out of 1140 potential articles, 21 met the inclusion criteria. Among the 4572 patients, 2687 and 1885 patients in the TLA and RSA groups, respectively. No significant differences were found in CSF leak (odds ratio [OR] 1.03; 95% confidence interval [CI] 0.81,1.32; P = .794) or meningitis (OR 1.05; 95% CI 0.45, 2.43; P = .73). Meta-regression showed no association with CSF leak and the number of cases per center or publication year. The TLA is associated with a shorter LOS (MD -1.20; 95% CI -1.39, -1.01; P < .01) and a higher chance of having and HB 4 or lower compared to patients who underwent RSA (OR 0.30; 95% CI 0.10, 0.89; P = .03).

Conclusion: There was no difference in the odds of CSF leak or meningitis between the groups. In addition, the TLA has a shorter LOS and a higher chance of a better facial nerve outcome compared to the RSA.

Meta-Analysis > J Neurooncol. 2025 Apr;172(2):347-359. doi: 10.1007/s11060-024-04935-5. Epub 2025 Feb 19.

Tinnitus after treatment of vestibular schwannoma: a systematic review and comparative analysis of microsurgery and stereotactic radiosurgery

Ramkumar Govindaraj [1] [2], Courtney Chambers [3], Marcus Kha [3], Thomas Sullivan [4] [5], Sharad Chawla [6], Andrew Zacest [7] [8], Peter Gorayski [3] [9] [10] [11], Daniel Roos [3] [7]

Affiliations + expand

PMID: 39969785 PMCID: PMC11937193 DOI: 10.1007/s11060-024-04935-5

Abstract

Purpose: The purpose of this systematic review and meta-analysis was to compare tinnitus outcomes following microsurgery and stereotactic radiosurgery for vestibular schwannoma.

Methods: The databases MEDLINE (via Ovid), EMBASE (via Ovid), Cochrane Central Register of Controlled Trials (via Ovid), SCOPUS, CINAHL (EBSCO), and Web of Science were searched for studies comparing microsurgery and radiosurgery treatment, and reporting tinnitus outcomes. Longitudinal tinnitus assessment with pre-treatment evaluation was required for inclusion. Fractionated radiotherapy treatment was excluded. Newcastle-Ottawa scale was used to assess the quality of the included studies. A separate random-effects meta-analysis was performed for the continuous, binary and ordinal tinnitus outcomes, with pooled effects described as a standardised mean difference or a log odds ratio as appropriate.

Results: Thirteen studies involving 5814 patients were included in the review; 4 were prospective studies, and the rest were retrospective cohort studies. The median follow-up duration in the microsurgery and radiosurgery groups was 39.5 months and 41.1 months, respectively. Studies were diverse with respect to inclusion criteria and method of tinnitus outcome assessment. Only 4 studies reported tinnitus scores using tinnitus questionnaires, while others used Likert scale, visual analogue scale, binary (present or absent) scale or ordinal (improved, same or worse) scale. Four studies reported better tinnitus outcomes after microsurgery than radiosurgery. However, the overall quality of the studies was low, and most did not control for important confounders, such as age, tumour characteristics, and hearing impairment. Meta-analysis of continuous and binary tinnitus outcomes showed no difference between the interventions (standardised mean difference = -0.04, 95% CI -0.37 to 0.28, p = 0.80; log odds ratio = 0.32, 95% CI -1.11 to 1.74, p = 0.66). Meta-analysis of tinnitus outcomes on an ordinal scale showed microsurgery increased the odds of reporting improved tinnitus compared to radiosurgery (log odds ratio = 0.83, 95% CI 0.01 to 1.64, p = 0.045). Heterogeneity between the studies was high for all outcome measures (I^2 > 56%).

Conclusion: Meta-analyses of tinnitus outcomes were largely inconclusive, except when tinnitus was reported as an ordinal outcome, which favoured microsurgery. However, due to the low quality of studies and high heterogeneity, no definitive conclusions could be drawn favouring either treatment.

Meta-Analysis > BMC Neurol. 2025 Sep 26;25(1):385. doi: 10.1186/s12883-025-04093-9.

Machine learning-based models in prediction of the radiological outcomes of vestibular schwannoma following stereotactic radiosurgery: a systematic review and meta-analysis

Bardia Hajikarimloo [1], Mohammad Ali Nazari [2], Mohammad Amin Habibi [3], Pourya Taghipour [4], Seyyed-Ali Alaei [5], Amirreza Khalaji [6], Rana Hashemi [7], Ibrahim Mohammadzadeh [8], Salem M Tos [9]

Affiliations + expand

PMID: 41013393 PMCID: PMC12465916 DOI: 10.1186/s12883-025-04093-9

Abstract

Background: Prediction of the radiological outcomes of the vestibular schwannomas (VSs) following stereotactic radiosurgery (SRS) is critical in the management of these lesions. Predictions of tumor control can optimize therapeutic strategies and enhance treatment outcomes. Significant advancements in machine learning (ML) have led to the development of models to predict the radiological outcomes after SRS in VS individuals. This study evaluated the role of ML-based models in predicting the radiological outcomes of SRS in the setting of VS.

Methods: On December 12, 2024, the four electronic databases, Pubmed, Embase, Scopus, and Web of Science, were systematically searched. Studies that evaluated the performance outcomes of the ML-based predictive models were included. The pooled sensitivity, specificity, area under the curve (AUC), and diagnostic odds ratio (DOR) were calculated through the R program. The hierarchical summary receiver operating characteristic (HSROC) model was utilized to form a summary ROC (SROC) curve.

Results: Nine studies with 1095 patients were included. Most of the best performance models were ML-based (88.9 8/9). The most frequent algorithm was the support vector machine (SVM) (44.4%, 4/9). The meta-analysis revealed a pooled sensitivity rate of 86% (95%CI: 83-89%), a specificity rate of 78% (95%CI: 62-89%), and a DOR of 19.8 (95%CI: 9.12-42.9). The SROC curve exhibited an AUC of 0.845 for tumor response prediction.

Conclusion: Clinical application of ML-based predictive models can optimize the therapeutic strategy and enhance the outcomes for patients with VS.

Meta-Analysis > World Neurosurg. 2025 Feb:194:123304. doi: 10.1016/j.wneu.2024.10.033. Epub 2024 Nov 14.

Stereotactic Radiosurgery in Primary Treatment of Sporadic Small to Medium (<3 cm) Vestibular Schwannomas: A Systematic Review and Meta-Analysis

Bryce J Bonin [1], Scott Beckman [1], Sultan Mahmud [2], Danielle Terrell [1], Stephen Garrett Whipple [1], Ryan Diaz [1], Mohammad Alfrad Nobel Bhuiyan [3], Deepak Kumbhare [1], Chiachien Jake Wang [4], Bharat Guthikonda [1], Amey R Savardekar [5]

Affiliations + expand

PMID: 39461420 DOI: 10.1016/j.wneu.2024.10.033

Free article

Abstract

Objective: To analyze the literature regarding the use of stereotactic radiosurgery as the primary treatment of vestibular schwannoma to further evaluate efficacy and treatment-related neurologic deficits.

Methods: Online databases were queried to identify relevant studies from January 2001 to December 2020. Full-text articles in English for sporadic vestibular schwannoma treated primarily with radiosurgery and documented hearing preservation data were reviewed. Studies that had a minimum follow-up period of less than 36 months, did not use radiosurgery for primary treatment, or included patients with neurofibromatosis type 2 were excluded.

Results: A total of 33 studies involving 4286 patients with an average follow-up of 62.5 months were included in the final analysis. All 33 studies included eligible hearing data; overall preservation of serviceable hearing was found to be 58.27%. Twenty-seven studies with 3822 eligible patients were analyzed for tumor control rates; overall, tumor control was reported in 92.98% of cases. Twenty-seven studies were analyzed for posttreatment facial nerve dysfunction, which was reported in 1.53% of cases.

Conclusions: Stereotactic radiosurgery is a safe and effective primary treatment modality for sporadic vestibular schwannoma as shown by the present analysis. Radiosurgery is effective regarding tumor control and hearing preservation and offers a low rate of posttreatment facial nerve dysfunction.

Meta-Analysis > BMC Cancer. 2025 Apr 15;25(1):698. doi: 10.1186/s12885-025-13959-7.

Stereotactic radiosurgery for vestibular schwannomas in neurofibromatosis type 2: a systematic review and meta-analysis

Bardia Hajikarimloo [1], Salem M Tos [2], Mohammadamin Sabbagh Alvani [3], Alireza Kooshki [4], Ibrahim Mohammadzadeh [5], Mohammad Amin Habibi [6]

Affiliations + expand

PMID: 40234793 PMCID: PMC11998438 DOI: 10.1186/s12885-025-13959-7

Abstract

Background: Management of neurofibromatosis type 2 (NF2)- associated vestibular schwannomas (VSs) is challenging due to their multiplicity, early onset, proximity to the brainstem, unpredictable growth, and aggressive behavior. The optimal therapeutic intervention remains controversial in the literature, and the advantages and disadvantages of each treatment option should be evaluated for each patient. Stereotactic radiosurgery (SRS) has exhibited favorable results in the management of NF2-associated VSs. This systematic review and meta-analysis aimed to assess the role of SRS in NF2-associated VSs.

Methods: On August 22, 2024, four electronic databases, comprising PubMed, Embase, Scopus, and Web of Science, were comprehensively searched. Studies that assessed SRS's radiological and clinical outcomes in NF2-associated VSs were enrolled.

Results: Nineteen studies were included with 960 individuals and 1310 NF2-associated VSs. The analysis showed a pooled local control (LC) rate of 83% (95%CI:74-90%). Older age (P = 0.001), prior resection (P = 0.003), and lower tumor volume (P = 0.019) were associated with higher LC rates. The results demonstrated a pooled serviceable hearing preservation (SHP) rate of 42% (95%CI:34-51%), trigeminal nerve worsening rate of 2% (95%CI:1-4%), and a facial nerve worsening rate of 5% (95%CI:2-9%). None of the patients experienced radionecrosis (RN) following SRS. Sensitivity analyses revealed a moderate to high robustness of the results. No publication bias was identified.

Conclusion: SRS is an effective therapeutic modality for managing VSs, especially small-to medium-sized lesions. We showed that SRS is associated with favorable LC and SHP rates and considerably low trigeminal or facial nerve worsening and RN rates.

Review > Cancers (Basel). 2025 Feb 4;17(3):519. doi: 10.3390/cancers17030519.

Efficacy and Toxicity of Bevacizumab in Children with NF2-Related Schwannomatosis: A Systematic Review

Annemijn L Tops [1], Josefine E Schopman [2], Radboud W Koot [3], Hans Gelderblom [2], Nabila A Putri [4], Latifah N A Rahmi [5], Jeroen C Jansen [1], Erik F Hensen [1]

Affiliations + expand

PMID: 39941885 PMCID: PMC11817438 DOI: 10.3390/cancers17030519

Abstract

Background/objectives: NF2-related schwannomatosis (NF2) is a tumor predisposition syndrome that typically presents with bilateral vestibular schwannomas, together with other intracranial and spinal schwannomas, meningiomas, and/or ependymomas. Bevacizumab, a VEGF inhibitor, has the potential to decrease schwannoma volume and improve hearing in adults, but the literature on the effects in children is sparse. This narrative review aims to evaluate the use of bevacizumab in pediatric NF2 patients, focusing on hearing, tumor progression, and toxicity.

Methods: A literature review was conducted following PRISMA guidelines. Articles were searched in PubMed, Embase, Web of Science, Cochrane Library, Emcare, and Academic Search Premier on 18 July 2024. Inclusion criteria were patients ≤ 18 years, diagnosed with NF2 and treated with bevacizumab. Two authors independently assessed the quality of the evidence and extracted relevant data from the included articles.

Results: Seventeen articles including 62 pediatric NF2 patients met the inclusion criteria. Studies varied widely in treatment regimens and outcome parameters. Tumor regression was reported in 6/56 patients (11%) and 38/56 (68%) remained stable. Hearing improved in 15/45 patients (33%) and did not further deteriorate in 27/45 (60%). An improvement in other symptoms was seen in 6/29 patients (28%). Toxicity was reported in five studies, documenting 13 adverse events in 28 patients ranging from grade 1 to grade 3. Treatment was discontinued in both patients who experienced grade 3 toxicity.

Conclusions: Bevacizumab seems to be a viable treatment option for pediatric NF2 patients. Tumor regression or stabilization is achieved in the majority of patients (77%). Moreover, a considerable number of pediatric patients experience hearing stabilization or improvement (93%). Bevacizumab appears to be relatively well tolerated, offering a non-invasive therapeutic option for children with NF2 suffering from progressive vestibular schwannomas and hearing loss.

Clinical Trial > J Neurooncol. 2025 Jul;173(3):751-757. doi: 10.1007/s11060-025-05020-1. Epub 2025 May 28.

Effect of bevacizumab on non-target intracranial meningiomas and non-vestibular schwannomas in NF2-related schwannomatosis: NF104

Vihang Nakhate [1], Ina Ly [1], Alona Muzikansky [1], Otto Rapalino [2], Jeffrey C Allen [3], Jaishri O Blakeley [4], Jian L Campian [5], D Wade Clapp [6], Girish Dhall [7], Rakesh K Jain [8], Matthias A Karajannis [9], Roger J Packer [10], James Tonsgard [11], Nicole J Ullrich [12], Bruce R Korf [7], Michael J Fisher [13], Scott R Plotkin [14, 15]; Neurofibromatosis Clinical Trials Consortium

Affiliations + expand

PMID: 40434540 DOI: 10.1007/s11060-025-05020-1

Abstract

Purpose: Bevacizumab treatment is associated with imaging and hearing responses in progressive vestibular schwannoma (VS) caused by NF2-related schwannomatosis (NF2-SWN). However, its effect on co-existing intracranial non-vestibular schwannomas (NVS) and meningiomas is unclear.

Methods: We retrospectively analyzed tumor volumes of non-target intracranial NVS and meningiomas in patients with NF2-SWN and progressive VS who were prospectively treated with bevacizumab for two years on the Neurofibromatosis Clinical Trials Consortium (NFCTC) trial NF104 (NCT01767792). Radiographic response (RR) or progression (PD) were defined as ≥ 20% decrease or ≥ 20% increase in tumor volume compared to baseline, respectively. All other responses were defined as stable disease.

Results: A total of 40 meningiomas in eight patients and 12 NVS in six patients were evaluated across 22 enrolled trial participants. On best response analysis, RR occurred in 13% (5/40) of meningiomas and in 42% (5/12) of NVS. On a per-patient basis, RR for meningioma occurred in 38% (3/8) of patients and for NVS in 67% (4/6) of patients. RR in two NVS were durable throughout the study period. During two years of treatment, PD occurred in 55% (22/40) of meningiomas and in 8% (1/12) of NVS. Median time to tumor progression was 15 months for meningiomas and was not reached for NVS.

Conclusions: We observed greater activity of bevacizumab against intracranial NVS compared to meningioma, evidenced by more favorable RR rates, durability of response, and rates of PD. Potential biological differences between meningiomas and schwannomas that underlie this differential response to bevacizumab warrant further investigation.

Meta-Analysis > J Clin Neurosci. 2025 Jul:137:111330. doi: 10.1016/j.jocn.2025.111330. Epub 2025 May 22.

"Salvage surgery for vestibular schwannomas after failed stereotactic radiosurgery or radiation: A systematic review and meta-analysis"

Filipe Virgilio Ribeiro [1], Marcelo Porto Sousa [2], Marcio Yuri Ferreira [3], Filipi Fim Andreão [2], Lucca B Palavani [4], Luis F Fabrini Paleare [5], Gabriel Simoni [6], Eduardo Corrêa [7], Christian Ken Fukunaga [8], Lucas Pari Mitre [9], Rafaela Hamada Jucá [10], Rudolfh Batista Arend [11], Bruno Zilli Peroni [11], Alex Roman [11], Raphael Bertani [12], Herika Negri Brito [13], Allan Dias Polverini [14]

Affiliations + expand

PMID: 40409174 DOI: 10.1016/j.jocn.2025.111330

Abstract

Introduction: Stereotactic radiosurgery effectively controls vestibular schwannoma (VS). However, in certain cases, microsurgical resection may be necessary for tumor progression after radiosurgery or, after failure of the latter. The results on the safety and efficacy of salvage surgery for VS are still unclear, with scarce literature on the subject.

Objective: The present study aimed to evaluate the safety and efficacy of salvage surgery on the resection of vestibular schwannomas that have been previously treated with stereotactic radiosurgery or radiotherapy.

Methods: Following PRISMA guidelines, we searched Medline, Embase, and Web of Science databases. We used single proportion analysis with 95 % confidence intervals under a random-effects model, I^2 to assess heterogeneity, and Baujat and sensitivity analysis to address high heterogeneity. Eligible studies included those with ≥ 4 patients treated with salvage surgery to resection of vestibular schwannomas after failure of stereotactic radiosurgery or radiotherapy.

Results: Of the 1841 initially identified studies, 18 were selected, involving 455 patients, with a median follow-up of 33 months. The combined analysis showed a 69 % (CI: 58 % - 79 %) rate of good clinical outcomes. Regarding partial resection, the pooled analysis confirmed a 48 % rate (CI: 33 % to 63 %) and a 52 % complete resection rate (CI: 37 % to 67 %). The pooled analysis confirmed a 95 % hearing preservation rate in patients undergoing the retrosigmoid approach (CI: 90 % to 100 %) and a 78 % facial nerve preservation rate (CI: 72 % to 84 %). Regarding complications, the pooled analysis confirmed a 20 % complication rate (CI: 14 % to 28 %). There were no deaths related to the procedure.

Conclusion: Based on the results, our meta-analysis identified that rescue surgery has been shown to be safe and effective for resection of vestibular schwannomas after failure of stereotactic radiosurgery or radiotherapy, based on good facial nerve preservation rate and total lesion resection rate.

Neurooncol Adv. 2025 Apr 24;7(1):vdaf083. doi: 10.1093/noajnl/vdaf083. eCollection 2025 Jan-Dec.

Phase II study of axitinib in patients with *NF2*–related schwannomatosis and progressive vestibular schwannomas

Mekka R Garcia [1], Mari Hagiwara [2], Anna Yaffe [3], Carole Mitchell [3], Srivandana Akshintala [3], Theodore Nicolaides [3], Sheetal S Phadnis [3], Kaleb Yohay [1], Yang Feng [4], Judith D Goldberg [5], Jeffrey C Allen [1], Matthias A Karajannis [6]

Affiliations + expand

PMID: 40575410 PMCID: PMC12199335 DOI: 10.1093/noajnl/vdaf083

Abstract

Background: Axitinib is an oral multi-receptor tyrosine kinase inhibitor targeting vascular endothelial growth factor receptor (VEGFR), platelet-derived growth factor receptor (PDGFR), and c-KIT. These represent a clinically and/or preclinically validated molecular targets in vestibular schwannoma (VS).

Methods: Eligible patients were age > 5 years with a clinical diagnosis of *NF2*-related schwannomatosis (*NF2*-SWN) and at least one volumetrically measurable, progressive VS. Axitinib was given continuously in 28-day cycles for up to of 12 cycles. Primary endpoint was objective volumetric response rate to axitinib, hearing response was a secondary endpoint, along with validated quality of life assessments (NFTI-QOL).

Results: Twelve patients were enrolled and 8 completed 12 cycles, including 2 pediatric patients. Ten patients were evaluated for the primary endpoint, defined as ≥ 20% decrease in VS volume, with 2 volumetric responses observed; both were reached after 3 cycles and sustained during treatment. The best volumetric response was -53.9% after 9 cycles. Three hearing responses were observed, one of which was sustained during treatment. All patients experienced drug-related toxicities, the most common were diarrhea, hematuria, and skin toxicity, not exceeding grade 2, as well as hypertension, not exceeding grade 3. NFTI-QOL scores remained stable or improved during treatment.

Conclusions: Axitinib therapy targeting VEGFR, PDGFR and c-KIT is feasible in this population and associated with volumetric and hearing responses in a subset of patients. However, convenience of oral administration should be balanced with respect to efficacy and safety of axitinib in comparison with other molecular-targeted therapies, including intravenous bevacizumab.