Journée scientifique SNOB
Société de
Neuro-Oncologie Bretonne

Actualités en Neuro-Oncologie

Docteur Elodie VAULEON

Vannes, le 09/10/2026

Actualités en Neuro-Oncologie

- **Présentations lors congrès 2026**
- **Publications de 2026**
- 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
- METASTASES CEREBRALES
- SCHWANNOME VESTIBULAIRE

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Centre Eugène Marquis RENNES

2026 ASCO ANNUAL MEETING

COGNO NHMRC Clinical Trials Centre

MAGMA: Multi-Arm GlioblastoMa Australasia Trial

COGNO MAGMA Consortium

Australian Brain Cancer Mission

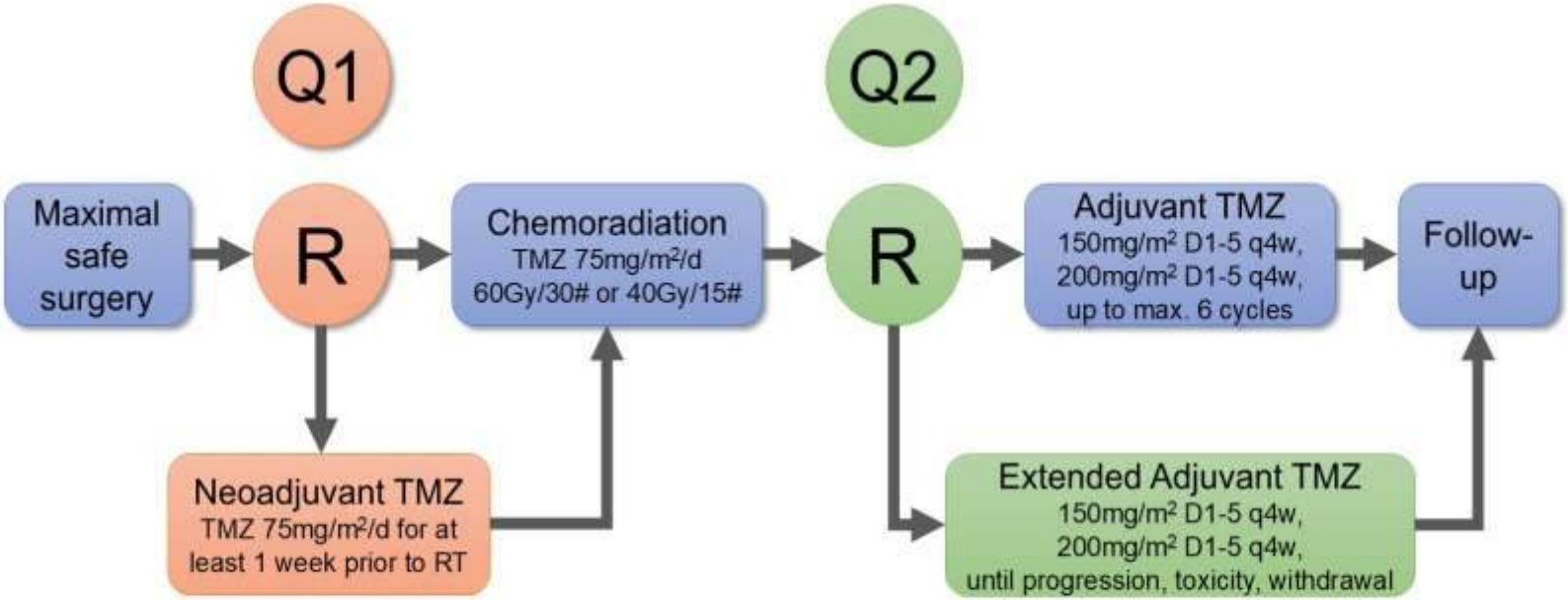
Medical Research Future Fund

CARRIE'S BLADES 4 BRAIN CANCER

MHF MARK HUGHES FOUNDATION

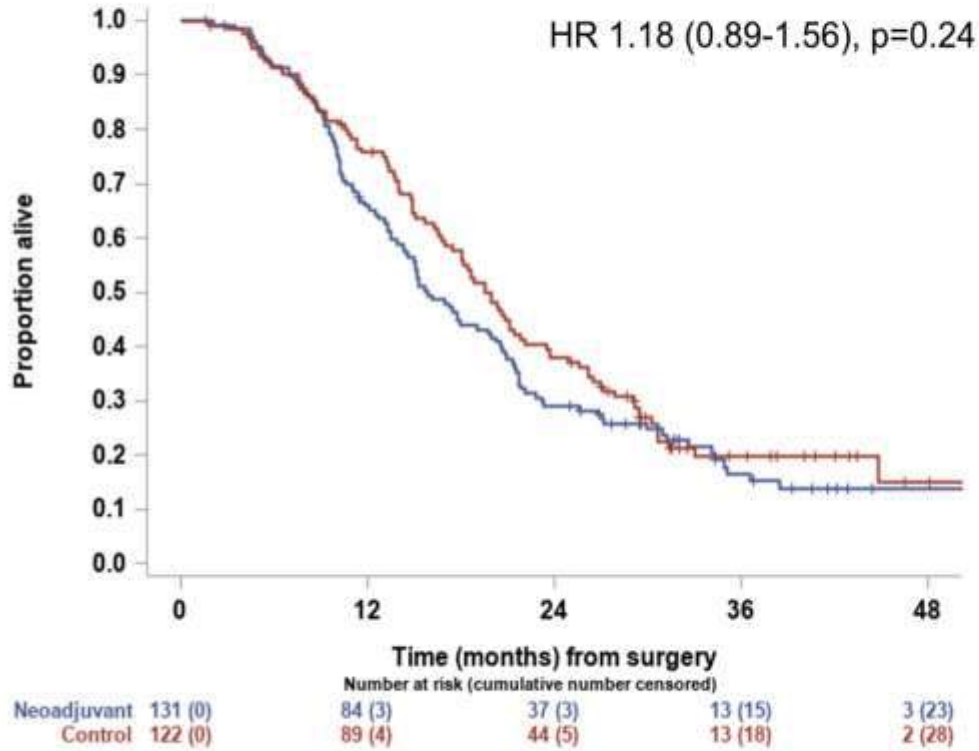
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Interventions



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Neoadjuvant TMZ does not improve OS



	OS	95%CI	PFS	95%CI
Neoadjuvant	16	14-20	8	7-9
Control	20	17-22	9	7-12

2026 ASCO ANNUAL MEETING #ASCO26

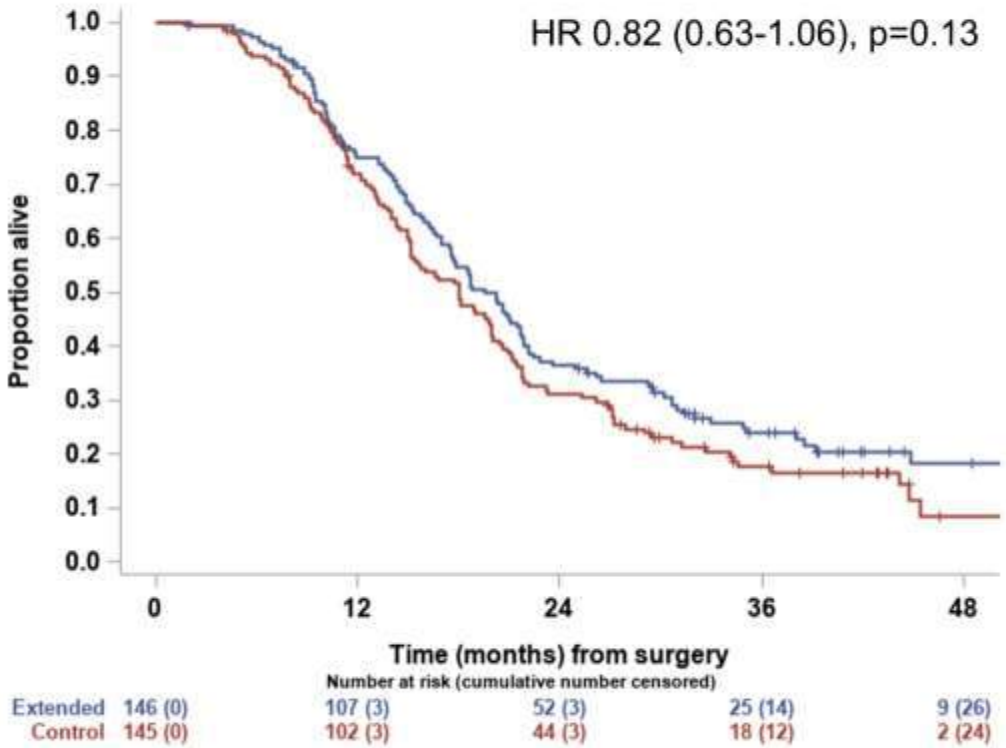
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ASCO KNOWLEDGE CONQUERS CANCER

En attente résultats STRATEGLIO

Extended TMZ does not improve OS

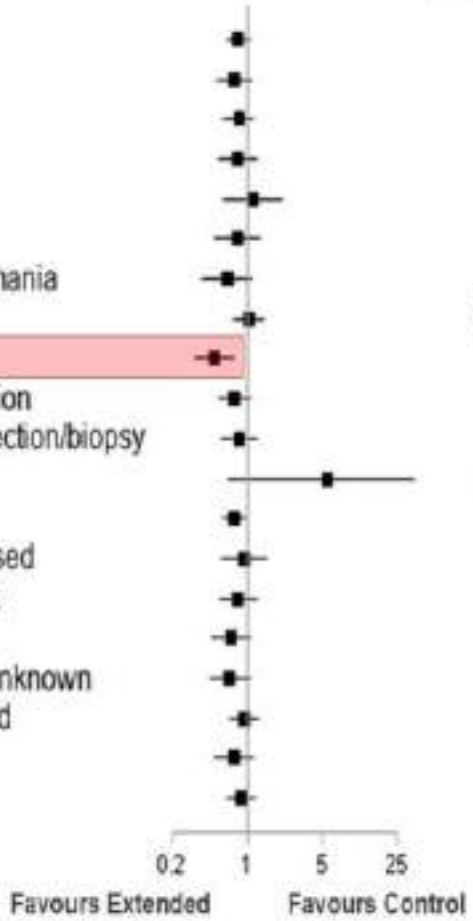


	OS	95%CI	PFS	95%CI
Extended	20	17-22	9	8-9
Control	18	15-20	9	7-10

Pas de données 12 vs 6 cycles

Subgroup analysis of Extended TMZ

Subgroup	Level	Interaction P-value
All participants	All	
Surgery to randomisation	<=8 weeks	0.70
	>8 weeks	
Site (grouped)	NSW	0.60
	Victoria	
	Queensland	
	SA/WA/Tasmania	
Age	<65	0.0028
	>=65	
Surgery	Gross resection	0.64
	Subtotal resection/biopsy	
IDH	Mutated	0.064
	Wild-type	
Q1 randomisation	Not randomised	0.80
	Neoadjuvant	
	Control	
MGMT	Methylated/unknown	0.33
	Unmethylated	
ECOG	0	0.60
	1, 2	

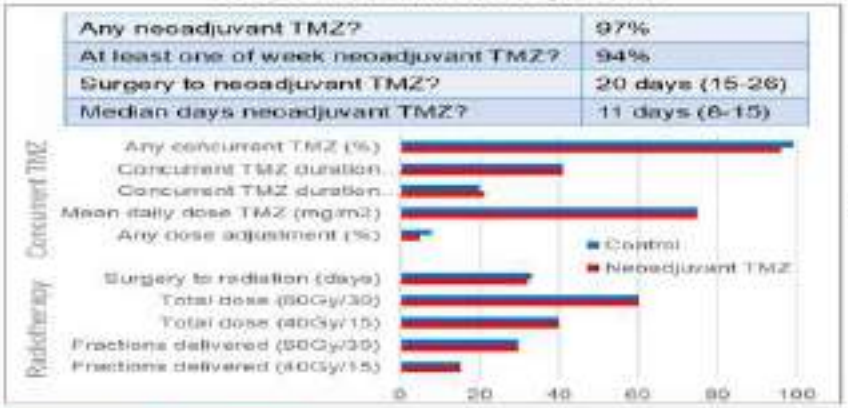


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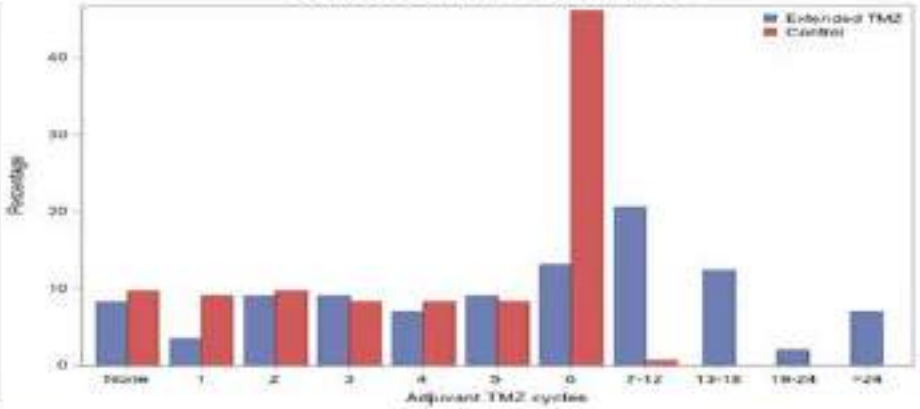
Treatment Received

Question 1: Neoadjuvant

Any neoadjuvant TMZ?	97%
At least one of week neoadjuvant TMZ?	94%
Surgery to neoadjuvant TMZ?	20 days (15-26)
Median days neoadjuvant TMZ?	11 days (6-15)



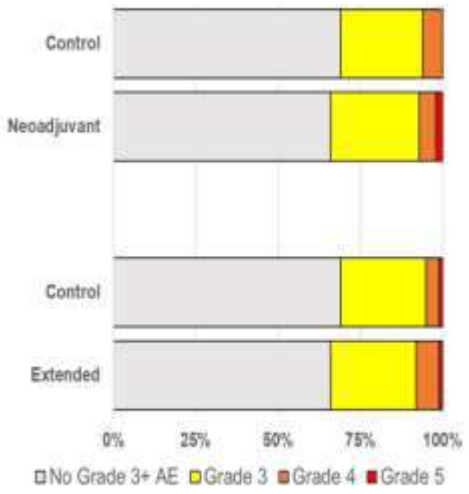
Question 2: Extended

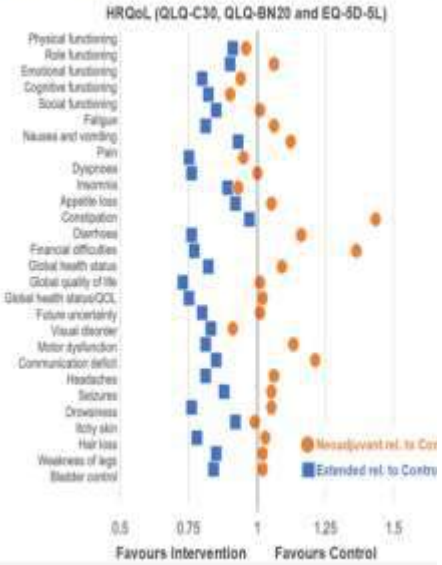


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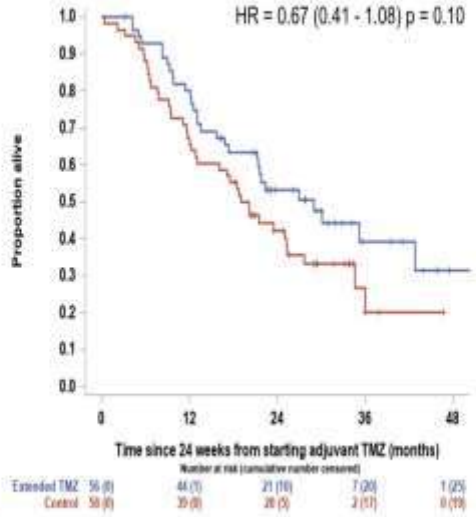
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Treatment Toxicity and Quality of Life





Landmark analysis of Extended TMZ



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2026 ASCO ANNUAL MEETING

Abstract Number: 2005

Clinicaltrials.gov id: NCT03212742

PHRC-K15-135 / INCa-DGOS_9780

Centre Baclesse

RÉPUBLIQUE FRANÇAISE

inca Institut National du Cancer

Phase 1/2A study of concomitant radiotherapy with Olaparib and Temozolomide in unresectable high-grade glioma patients – Final results from the phase 2A step (OLA-TMZ-RTE-01)

D. Stefan[1,12], J. Lequesne[1], P. Kubicek[2], M.P. Sunyach[3], Elisabeth Cohen-Jonathan Moyal[4], J. Jacob[5], M. Fontanilles[6,7], J. Geffrelot[1], M. Boone[8], J. Riverain[1], M. Ducloie[1,9], G. Braux[9], J. Lacroix[1], F. Missohou[1], M. Faisant[9], E. Emery[9], E. Girard[10], J.M. Grellard[1], P. Lesueur[11,13], B. Clarisse[1]

[1]Centre François Baclesse, Caen, Fr;[2]Institut de Cancérologie de l'Ouest, Angers, Fr;[3]Centre Léon Bérard, Lyon, Fr;[4]Oncopole Claudius Regaud, IUCT-Oncopole, Toulouse, Fr; [5]Pitié-Salpétrière, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, Fr; [6]Centre Henri Becquerel, Rouen, Fr; [7]UNIROUEN, Inserm U1245, IRON group, Normandy Centre for Genomic and Personalized Medicine, Normandie university, Rouen University Hospital, Rouen, Fr; [8]Amiens University Medical Center, Amiens, Fr; [9]CHU Côte de Nacre, Caen, Fr; [10]Groupe Hospitalier Bretagne Sud, Lorient, Fr;[11]Guillaume le Conquérant Center, Le Havre, Fr; [12]ABTE UR 4651, Normandie Univ, Caen, France, [13]ISTCT UMR6030-CNRS, CEA, Université de Caen-Normandie, Equipe CERVOxy, Caen, Fr.

Speaker : Dinu STEFAN, radiation oncologist, Comprehensive Cancer Centre François Baclesse, Caen, France

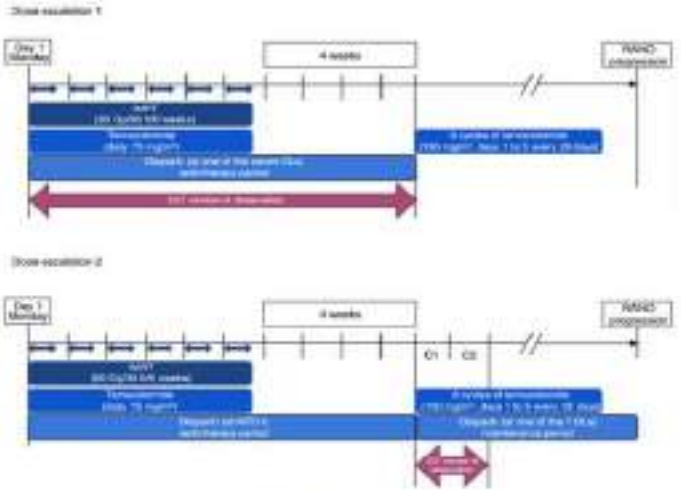
AstraZeneca

UR ABTE

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Methods _ OLA TMZ RTE 01 trial phase 1/2A study

- First study combining concomitant **radiotherapy, temozolomide,** and a ***PARP* inhibitor**
- **First-line treatment** of patients with **unresectable high-grade gliomas,** with or without *MGMT* promoter methylation
- **Multicenter, two-dose-escalation Phase 1, followed by a two-stage Phase 2A,** Lesueur Stefan et al, 2019 PMID: 30832617



- **Phase 1** (30 pts), Stefan et al 2025, PMID: 39882966
  - **Recommended Phase 2 dose of Olaparib : 100 mg Q12H for 3 days a week**, to be administered concurrently during both the **concomitant chemoradiotherapy** and **maintenance** periods of standard treatment

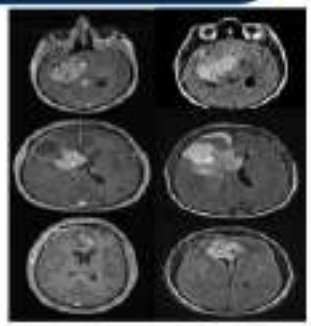
Results _ Patient characteristics

- **68 poor prognosis glioblastoma patients enrolled** from 2020 to 2024

	Total (N=68)
Sex Male	41 (60.3%)
Median Age	59 [20-70]
Histology	68 (100%)
Confirmed glioblastoma	66 (97%)
Anaplastic astrocytoma	2 (3%)
Quality of surgical resection	
Biopsy only	26 (38.2%)
Debulking	42 (61.8%)
GTR	0 (0%)
Molecular profile	
IDH1	1 (1.5%)
BRAF V600E	2 (2.9%)
Methylated MGMT	24 (35.3%)
FGFR fusion	5 (7.4%)
Met amplification	1 (1.5%)
MDM amplification	1 (1.5%)

- Median age ~60 years
- Unresectable tumors
- Good performance status at diagnosis
- Molecular profile consistent with historical cohorts

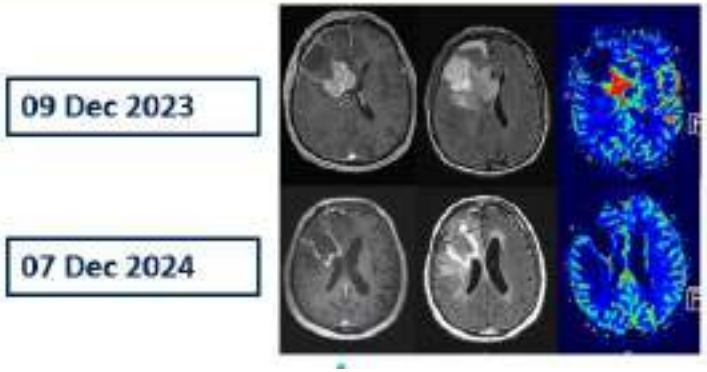
	Total (N=68)	
Tumor location		
Right	32	(47.1%)
Left	34	(50%)
Bilateral	2	(2.9%)
ECOG		
0	34	(50.7%)
1	28	(41.8%)
2	5	(7.5%)
Treatment Volume		
GTV median cm³ [min-max]	30.2	[14-64]
PTV median cm³ [min-max]	295	[216-348]

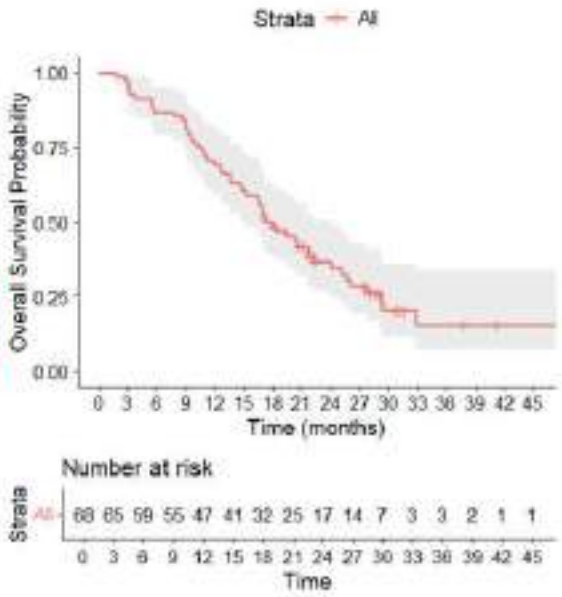


Results _ Primary endpoint (12-month Overall Survival)

Median Follow-up	All pts (N=68): **17.2** months (range 1.67- 61.1) Pts alive (N=17): **28.1** months (range 17.18 - 61.1)
Median OS	17.2 months ($_{95\%}$CI 14.7-22.3)
12-month OS rate	**69.1%** ($_{95\%}$ CI 59-81) **Z-statistic = 1.292 > 1.235**

Confirmation of the positive outcome of this study





Toxicity, N (%)	Grade 1-2	Grade ≥3
Anemia	10 (15)	4 (6)
Thrombocytopenia	22 (32)	5 (7)
Neutropenia	6 (9)	15 (22)
Lymphopenia	9 (13)	19 (28)
Febrile neutropenia	0	2 (3)
Fatigue	47 (69)	6 (9)
Nausea	33 (49)	0
Epilepsy/Seizure	5 (7)	5 (7)
Pulmonary embolism	0	5 (7)

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	EORTC-NCIC Stupp et al., 2005, 2009 PMID: 15758009 PMID: 19269895		EF-14 Stupp R et al., 2017, PMID: 29260225		OLA-TMZ-RTE-01 PMID: 39882966	
Trial	*prospective, randomized, multicentric phase III*		*prospective, randomized, multicentric phase III*		*prospective, multicentric phase 1-2A*	
	Radiotherapy alone vs radiotherapy plus concomitant and adjuvant temozolomide		Radiotherapy plus concomitant and adjuvant temozolomide vs adjuvant temozolomide and TTFields		Radiotherapy plus concomitant and temozolomide and Olaparib	
Median follow-up	28 & 60 months		40 months		17.2 months	
	Patients (%)	OS (standard vs experimental)	Patients (%)	OS (standard vs experimental)	Patients (%)	OS (experimental)
Total included patients	573 (100%)	12.1 vs 14.6 (PFS 5 vs 6.9)	695 (100%)	16 vs 20.9 (PFS 4 vs 6.7)	68	17.2 (PFS 4.5)
Biopsy only	88 (15%)	7.8 vs 9.4	89 (13%)	11.6 vs 16.5	26 (38%)	14.9
Debulking	239 (41%)	11.7 vs 13.5	234 (33%)	15.1 vs 21.4	42 (62%)	19
GTR	205 (35%)	14.2 vs 18.8	372 (53%)	18.5 vs 22.6	0 (0%)	-
IDH+	?	?	25 (3.5%)	?	1 (1.4%)	-
MGMT methylated	80 (14%)	15.3 vs 23.4	214 (30%)	21.2 vs 31.6	24 (35%)	25.1
MGMT unmethylated	108 (19%)	11.8 vs 12.6	304 (43%)	14.7 vs 16.9	29 (43%)	13.6
Age <50-65	172 (30%)	13.2 vs 17.4	561 (81%)	17.3 vs 21.6	54 (79%)	20.2
Age >50-65	401 (70%)	11.9 vs 13.6	134 (19%)	13.7 vs 17.4	14 (21%)	11.7

Key Takeaway Points/Conclusions

1

Olaparib combined with the Stupp protocol in unresectable glioblastoma

Median OS: 17.2 mo

12-mo OS rate: 69.1%

2

Manageable safety profile of intermittent Olaparib (100 mg Q12H 3 days/week) concomitant with the Stupp regimen

3

OS compares favorably to Stupp biopsy-only (14.9 vs 9.4 mo) and partial-resection (19 vs 13.5 mo) historical data, in a population with no GTR

This study provides the first phase 2 efficacy signal of Olaparib + Stupp protocol as first-line treatment of *unresectable HGG regardless of MGMT status*, supporting the rationale for a randomized phase 3 trial to confirm the benefit of *PARP* inhibition in this setting.

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> Lancet. 2026 Sep 25:S0140-6736(26)01804-0. doi: 10.1016/S0140-6736(26)01804-0. Online ahead of print.

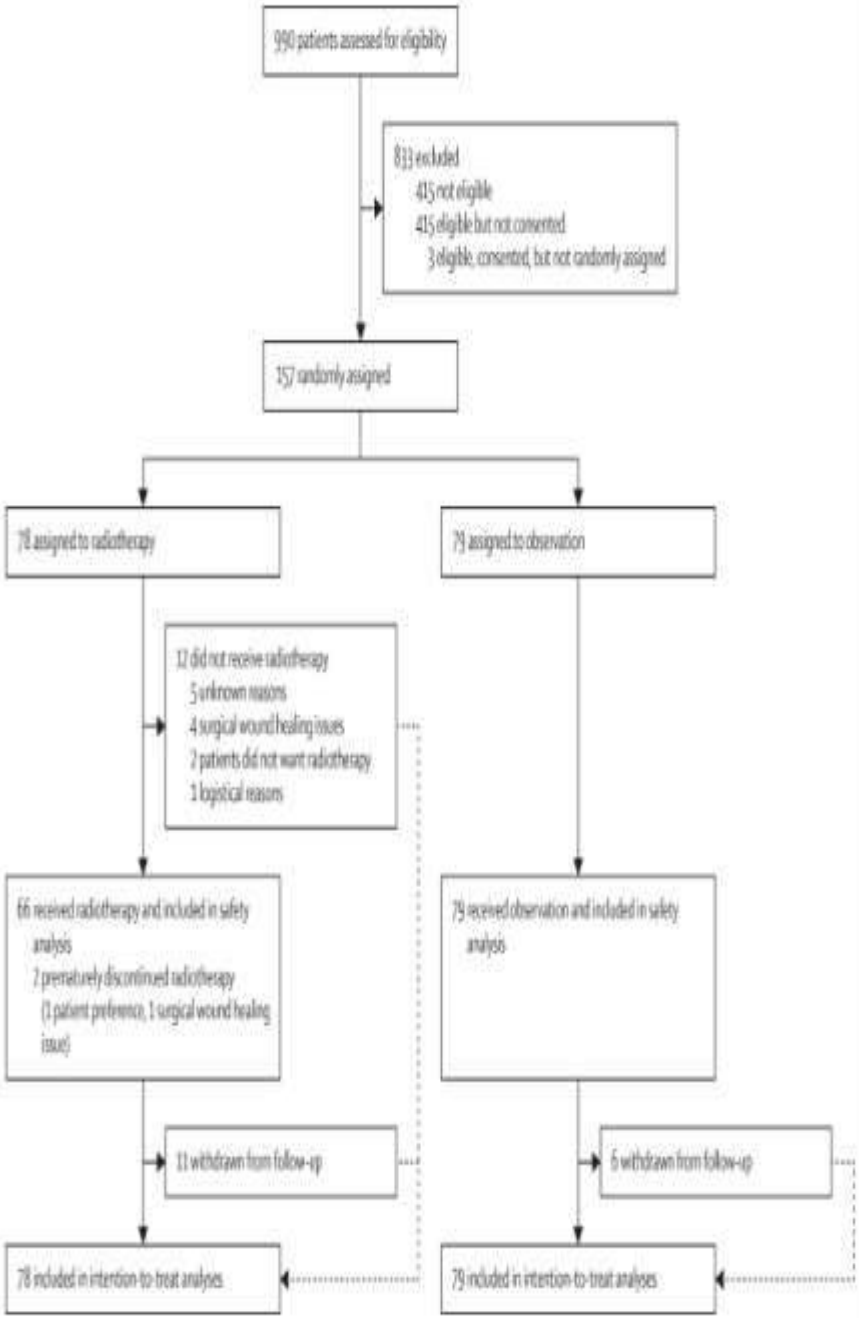
Radiotherapy versus observation following surgical resection of WHO grade 2 atypical meningioma (ROAM/EORTC-1308): an international, multicentre, open-label, phase 3, randomised controlled trial

Michael D Jenkinson [1], Anna Rosala-Hallas [2], Felix Sahm [3], Nicolaus Andratschke [4], Keyoumars Ashkan [5], Damiano Balestrini [6], Helen Bulbeck [7], Silvia Comas [8], Giovanna Culeddu [9], Kumar Das [10], Laura Fariselli [11], Karen Fowkerer [12], Priya Francis [2], Efstathia Gkioni [2], Vassilis Golfinopoulos [13], Thierry Gorlia [13], Neda Haghighi [14], Brian J Haylock [15], Dyfrig A Hughes [6], Mohsen Javadpour [16], Philippe Martinive [17], Helen M O Mayles [15], Perry Moore [18], Emilie Le Rhun [18], Nicola Rosenfelder [19], Gail Ryan [20], Michael Weller [21], Carrol Gamble [2], Matthias Preusser [22], Damien C Weber [23]; ROAM/1308 Study Collaborators

Collaborators, Affiliations + expand

PMID: 42790456 DOI: 10.1016/S0140-6736(26)01804-0

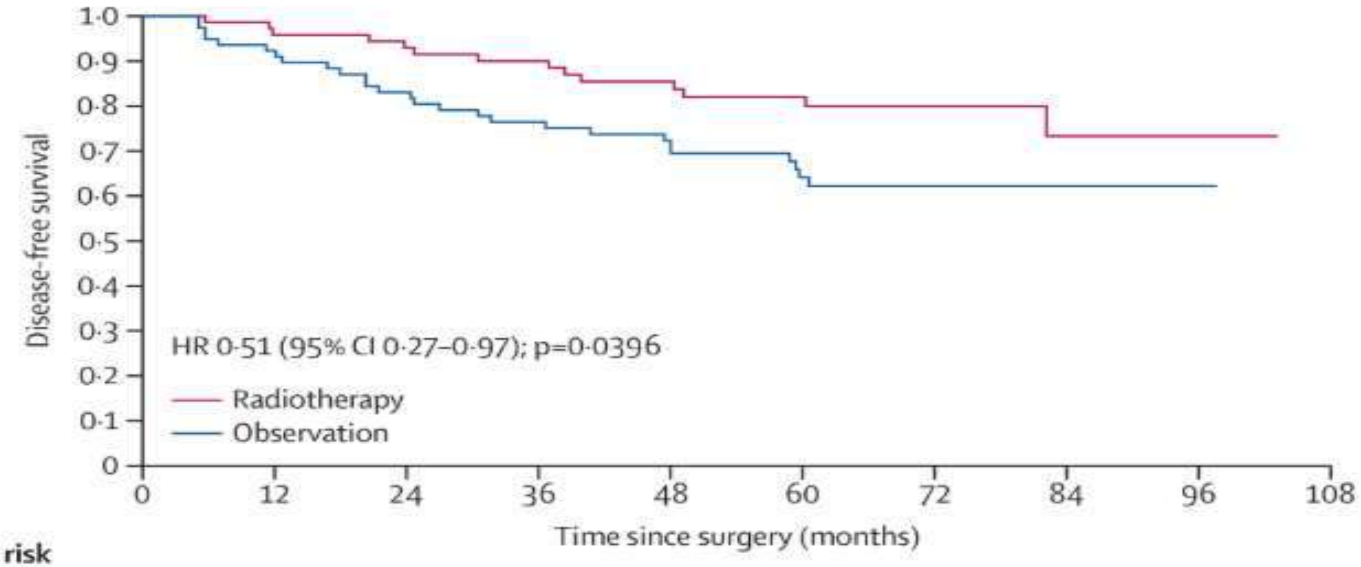
- **Background:** WHO grade 2 atypical meningioma is a primary brain tumour with a high risk of recurrence even after complete surgical resection. The role of adjuvant radiotherapy remains uncertain. We aimed to assess whether adjuvant radiotherapy reduces recurrence compared with observation in patients with a newly diagnosed atypical meningioma who have undergone complete surgical resection.
- **Methods:** ROAM/EORTC-1308 was an international, multicentre, open-label, phase 3, randomised controlled trial, conducted at 58 hospitals and academic centres in 11 countries. Eligible sites had appropriate multidisciplinary expertise, neurosurgery, and radiotherapy facilities. Patients aged 16 years or older who had undergone a surgeon-assessed complete surgical resection of newly diagnosed atypical meningioma were randomly assigned (1:1) to adjuvant radiotherapy or observation. Randomisation was done using a web-based interface using random variable blocks of sizes two and four, stratified by location (UK or non-UK). Participants assigned to the radiotherapy group received fractionated external-beam intensity-modulated radiotherapy at a total dose of 60 Gy in 30 fractions over 6 weeks. Participants were followed up for a minimum of 4 years. The primary outcome was disease-free survival, defined as time from surgery to MRI-confirmed recurrence or death due to any cause, analysed in all randomly assigned participants in their assigned treatment group. Harms analysis was done in the as-treated population. The trial was registered with ISRCTN, ISRCTN71502099, and has completed.
- **Findings:** Between April 28, 2016, and May 21, 2021, 990 patients were assessed for eligibility, 157 of whom were randomly assigned to radiotherapy (n=78) or observation (n=79). Median age was 57·40 years (IQR 49·09-66·93); 84 (54%) participants were female and 73 (46%) were male. At a median follow-up of 64 months (IQR 50-75), meningioma recurrence occurred in 11 (14%) of 78 participants in the radiotherapy group and 24 (30%) of 79 in the observation group. 5-year disease-free survival was 79·9% (95% CI 67·6-87·9) in the radiotherapy group and 64·3% (51·9-74·2) in the observation group (absolute difference 15·6% percentage points [95% CI 0·6-30·5]). Disease-free survival was improved in the radiotherapy group compared with the observation group (hazard ratio 0·51 [95% CI 0·27-0·97]; p=0·0396). Grade 2 or 3 radiation-related serious adverse events occurred in five (8%) of 66 participants in the radiotherapy group, with no treatment-related deaths.
- **Interpretation:** Our findings suggest that adjuvant radiotherapy should be considered in patients with atypical meningioma after complete surgical resection of atypical meningioma when the prevention of recurrence is valued higher than the potential delayed adverse effects of radiotherapy. This practice will benefit patients by reducing meningioma recurrence. Decisions should be based on individual discussion with the patient.



Characteristics of the intention-to-treat population at baseline

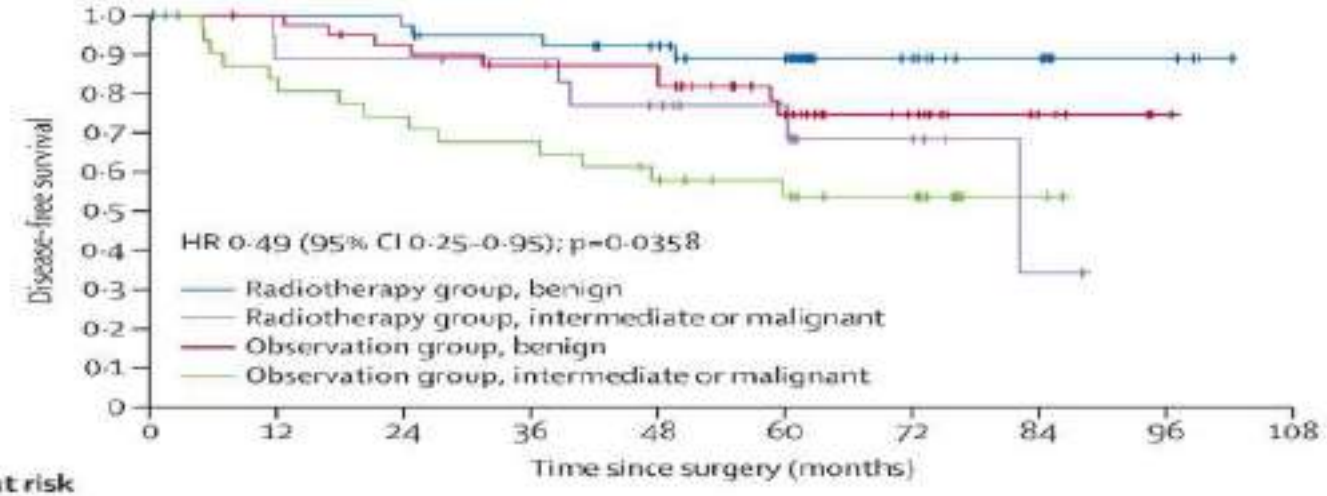
	Radiotherapy group (n=78)	Observation group (n=79)
Sex		
Female	41 (53%)	43 (54%)
Male	37 (47%)	36 (46%)
Age, years		
Median (IQR)	56·94 (49·29–64·38)	59·44 (48·01–68·92)
Range	33·36–77·40	26·44–77·06
WHO performance status		
0	42 (54%)	40 (51%)
1	31 (40%)	34 (43%)
2	5 (6%)	5 (6%)
Simpson grade		
Grade I	33 (42%)	39 (49%)
Grade II	37 (47%)	37 (47%)
Grade III	8 (10%)	3 (4%)
Tumour location		
N	70	75
Anterior cranial fossa	13 (19%)	7 (9%)
Convexity	23 (33%)	34 (45%)
Falcine or parasagittal	24 (34%)	16 (21%)
Posterior fossa	3 (4%)	4 (5%)
Sphenoid wing	5 (7%)	8 (11%)
Tentorial	2 (3%)	0
Other	0	6 (8%)
Missing	8	4
Seizures at presentation		
N	74	79
Yes	16 (22%)	18 (23%)
No	58 (78%)	61 (77%)
Missing	4	0

Data are n (%), unless otherwise specified.



Number at risk (censored)

Radiotherapy	78 (0)	68 (7)	65 (8)	60 (11)	52 (16)	41 (25)	23 (42)	11 (53)	4 (60)	0 (64)
Observation	79 (0)	71 (2)	63 (3)	57 (4)	51 (7)	36 (17)	23 (29)	8 (44)	1 (51)	0 (52)

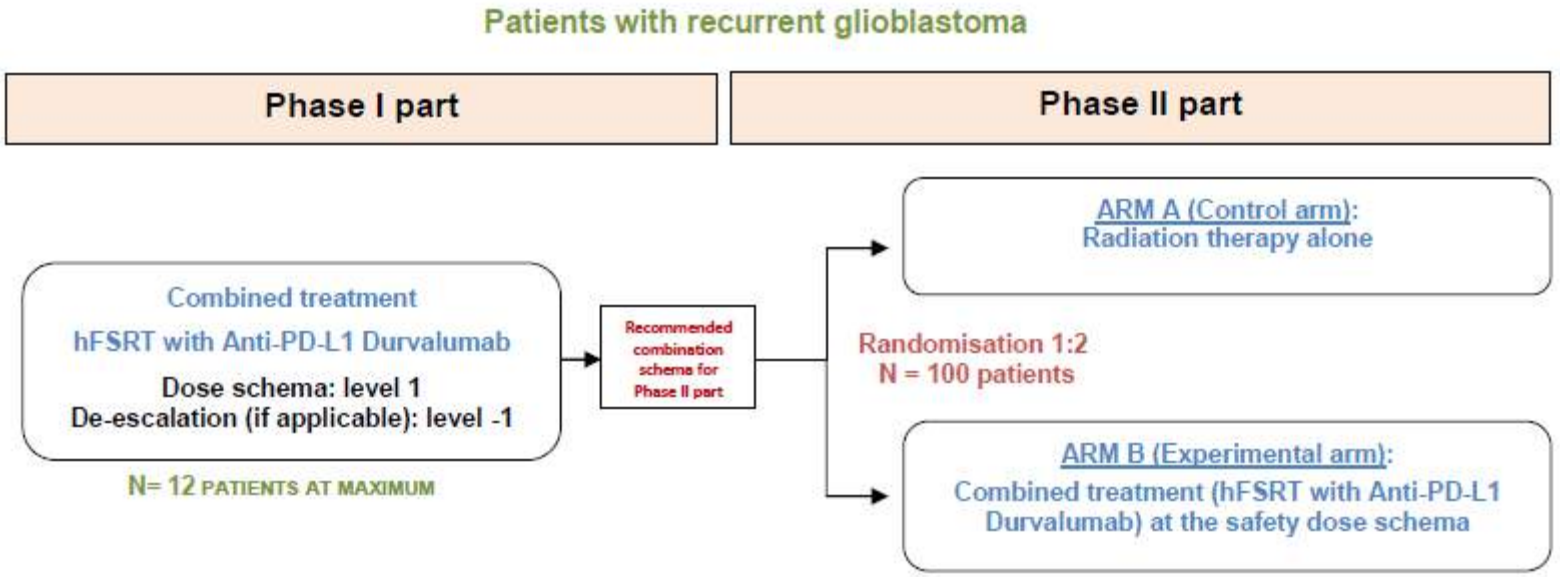


Number at risk (censored)

Radiotherapy group, benign	41 (0)	39 (2)	38 (2)	35 (4)	31 (7)	26 (11)	14 (23)	8 (29)	4 (33)	0 (37)
Radiotherapy group, intermediate or malignant	19 (0)	16 (1)	16 (1)	15 (2)	12 (3)	9 (6)	5 (9)	1 (12)	0 (13)	0 (13)
Observation group, benign	41 (0)	40 (1)	36 (2)	33 (3)	32 (4)	21 (11)	12 (20)	5 (27)	1 (31)	0 (32)
Observation group, intermediate or malignant	31 (0)	26 (0)	23 (0)	21 (0)	17 (1)	13 (4)	10 (7)	2 (15)	0 (17)	0 (17)

STERIMGLI trial : phase 2

- Lors du congrès mondial de neuro-oncologie **SNO 2025** Professeur Elizabeth Cohen-Moyal (de l'IUCT-Oncopole de Toulouse) s'est vu décerner le prestigieux Prix de l'étude clinique 2025 (Clinical Trial Award).



Hypo-fractionated stereotactic reirradiation with 24 Gy in 3 fractions plus durvalumab versus reirradiation alone inrecurrent glioblastoma: the comparative randomized phase 2 STERIMGLI trial

Background

Hypo-fractionated stereotactic radiotherapy (HFSRT) is a therapeutic option for recurrent glioblastoma. Its efficacy may be enhanced when combined with an immune checkpoint inhibitor to promote immunogenic cell death. We investigated whether HFSRT combined with anti-PD-L1 durvalumab versus HFSRT alone improved overall survival (OS) of patients with glioblastoma relapse.

Methods

This multicentric, open-label, randomized, controlled, phase 2 trial (ClinicalTrials.gov; NCT02866747) included relapsed glioblastoma patients (WHO 2016 classification) with tumor maximum size ≤35 mm, randomly assigned (1:2) to HFSRT alone (24 Gy in 3 fractions over 5 days, Arm A) or to the same HFSRT plus durvalumab (1500 mg on day 5, then every 4 weeks Arm B). The primary endpoint was overall survival with 77 events required to detect a Hazard Ratio (HR) of 0·57 at 85% power (one-sided, 10%-level test).

Findings

Patients (n=102) randomized to arm A (n=34) and B (n=68) had balanced baseline characteristics, except for prior targeted therapy (A=2·9% versus B= 22·1%) and IDH-mutated glioblastoma (A=15·6% versus B= 6·1%). Treatment was well-tolerated, with 12·4% of patients with a grade 3 treatment-related event (no grade ≥4). After a median follow-up of 34·1 months (95%CI 24·3;71·4), median OS was 13·3 months in arm A versus 16·1 months in arm B (HR=0·77, 80%CI 0·56;1·06, one-sided p=0·15). In multivariable exploratory post-hoc analysis, adjusted HR was 0·41 (80%CI 0·28;0·60). Among patients with IDH-wildtype glioblastoma (WHO 2021), median OS was 10·9 versus 16·1 months (HR=0·54, 80%CI 0·39;0·76, one-sided p=0·010). No clinically meaningful differences in quality-of-life or neurocognitive function scores were observed. Treatment-induced increase in plasma IFN-γ was associated with longer OS in arm B (adjusted HR 0·36, 95%CI 0·18–0·71; p=0·0034).

Interpretation

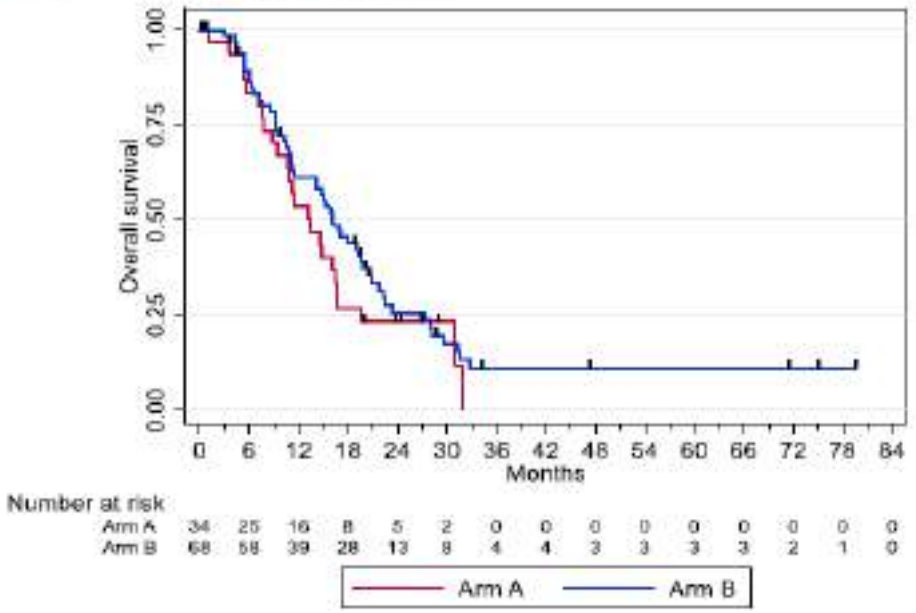
To the best of our knowledge, the STERIMGLI trial is the first randomized trial demonstrating an OS benefit of HFSRT reirradiation combined with durvalumab in IDH-wildtype glioblastoma patients at relapse.

- **Efficacy** *Primary endpoint*
- The median follow up was 34·1 months (95%CI 24·3-71·4), mOS (Figure 2A) was 13·3 months (80%CI
- 10·9-16·1) in arm A and 16·1 months (80%CI 14·3-19·2) in HFSRT-durvalumab arm B, hazard ratio
- (HR)=0·77 (80%CI 0·56-1·06), one-sided p=0·146.

- In multivariable exploratory post-hoc analysis adjusting for prognostic factors a significant difference
- between arms was observed with an adjusted HR of 0·41 (80%CI 0·28-0·60) (Table 3).

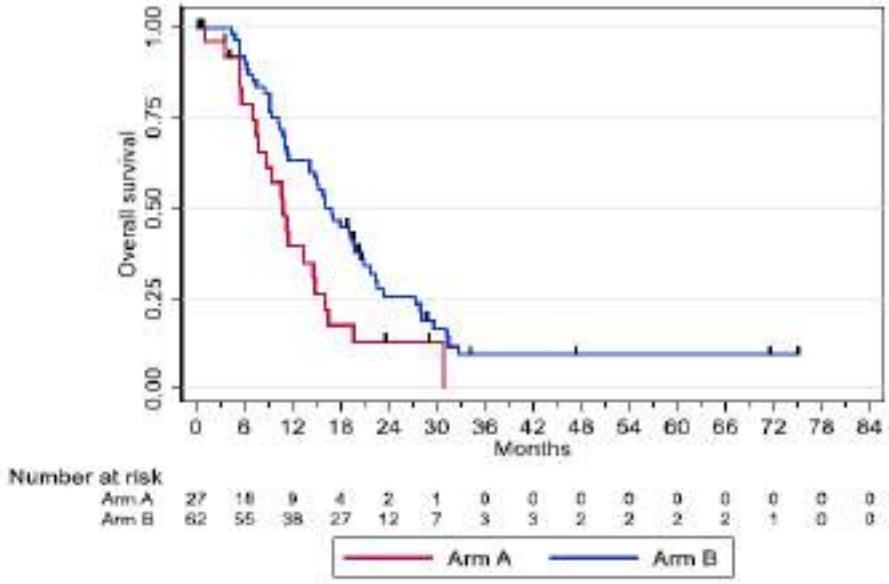
- Among patients with IDH-wildtype glioblastoma WHO 2021glioblastoma definition), median OS was
- 10·9 (80%CI 8·7-13·3) in arm A vs. 16·1 months (80%CI 14·9-19·2) in arm B (HR=0·54, 80%CI 0·39-
- 0·76, one-sided p=0·010) (Figure 2B). In the subgroup of patients relapsing within 24 months of the
- initial diagnosis, the OS was significantly longer in HFSRT+durvalumab treated patients HR=0·52
- (80%CI 0·35-0·77, one-sided p=0·016). As shown in Figure 3, neither MGMT promoter methylation
- status nor PD-L1 expression was associated with treatment response.

Figure 2A
HR 0·77 (80% CI 0·56-1·06); 1-sided p=0·15



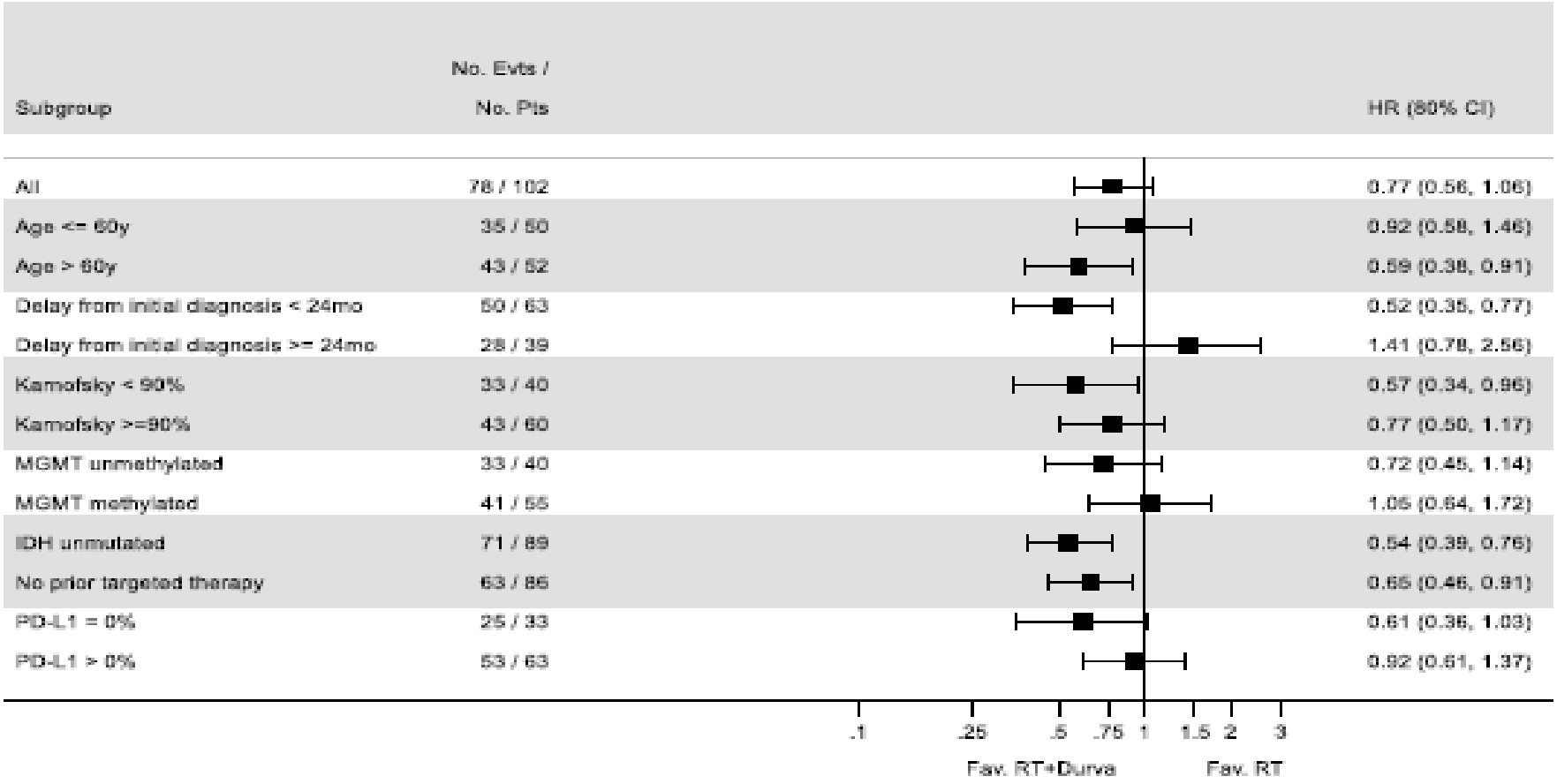
(2A) Kaplan Meier estimates for overall survival in all patients

Figure 2B
HR 0·54 (80% CI 0·39-0·76); 1-sided p=0·010



(2B) Kaplan Meier estimates for overall survival in glioblastoma IDH wild type subgroup

Analyse multivariée



- In the subgroup of patients relapsing within 24 months of the initial diagnosis, the OS was significantly longer in HFSRT+durvalumab treated patients HR=0·52 (80%CI 0·35-0·77, one-sided p=0·016). Neither MGMT promoter methylation status nor PD-L1 expression was associated with treatment response.

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- Tumeur de REGION PINEALE
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Centre Eugène Marquis RENNES

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

Honeyman SI, Boukas A, Akhbari M, Okoli B, Stacey R, Apostolopoulos V, Plaha P.

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

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.

unicancer

OS ↗ mais pas PFS, EOR mais pas GTR : Biais de sélection ?

Awake Craniotomy Versus General Anesthesia for Resection of High-Grade Gliomas: A Systematic Review and Meta-Analysis.

Nowacka A, Śniegocki M, Atkins W, Ziółkowska E.

J Clin Med. 2026 Feb 12;15(4):1431. doi: 10.3390/jcm15041431.

Background: The optimal anesthetic approach for high-grade glioma resection remains controversial. We conducted a systematic review and meta-analysis comparing awake craniotomy with intraoperative brain mapping versus general anesthesia for adults with high-grade gliomas. **Methods**: We searched PubMed/MEDLINE, Web of Science, Cochrane Library, and Embase databases from January 2000 to August 2025 for comparative studies of awake craniotomy versus general anesthesia in adults with WHO grade III-IV gliomas. Primary outcomes were overall survival and neurological deficits. Meta-analyses used random-effects models with hazard ratios (HR) for survival and risk ratios (RR) for binary outcomes. **Results**: Eleven studies comprising 2689 patients (854 awake craniotomy, 1835 general anesthesia) were included. One randomized controlled trial and ten observational studies met inclusion criteria. Awake craniotomy was associated with improved overall survival (HR 0.70, 95% CI 0.60-0.82; 4 studies, 1273 patients), representing a 30% reduction in mortality risk and a median survival advantage of approximately 4.1 months (18.5 vs. 14.4 months; low certainty evidence due to predominantly observational data and heterogeneity). Neurological deficits at 3 months were significantly reduced with awake craniotomy (RR 0.62, 95% CI 0.42-0.91; 2 studies, 1111 patients; moderate certainty evidence), with absolute deficit rates of 13% versus 21% (number needed to treat = 13). Awake craniotomy also achieved greater extent of resection (mean difference 4.4%, 95% CI 2.8-6.0%; 5 studies, 1121) and notably shorter hospital stay (mean difference -2.85 days, representing a 41% reduction [4.1 vs. 6.95 days]; 2 studies, 949 patients). Substantial heterogeneity was observed for most outcomes (I^2 > 50%). Subgroup analysis demonstrated greater benefits for tumors in eloquent areas. Limitations include predominantly observational studies with potential selection bias (including possible differences in baseline performance status), molecular marker heterogeneity due to evolving WHO classification systems, and one small randomized controlled trial showing opposite results. **Conclusions**: Awake craniotomy may offer survival and functional benefits for selected patients with high-grade gliomas, particularly those with tumors in eloquent areas. However, evidence certainty is limited by the observational nature of most studies and significant heterogeneity. Well-designed randomized trials with molecular stratification and performance status adjustment are needed to establish definitive evidence.

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Awake Craniotomy for Eloquent Region **Glioblastoma** Classified by Tumor Location-A Retrospective and Prospective Cohort Study.

Li Y, Weng S, Dong J, Wang J, Zhang Z, Fan X, Wang Y, Ma W, Jiang T, Fang S.

CNS Neurosci Ther. 2026 Sep;32(9):e71126. doi: 10.1002/cns.71126.

Introduction: The efficacy of awake craniotomy (AC) with intraoperative mapping for glioblastoma (GBM) in eloquent regions remains debated. This study aims to evaluate functional and survival outcomes of GBM patients undergoing AC stratified by tumor locations.

Methods: A combined retrospective (2015-2023, n = 114: 43 AC vs. 71 standard craniotomy) and prospective cohort (2023-2025, n = 28: 13 AC vs. 15 standard craniotomy) of GBM patients with motor/language-eloquent tumors was analyzed. Tumors were classified into motor subtypes (I: precentral gyrus; II: premotor/supplementary motor; III: internal capsule posterior limb; IV: other) and language subtypes (I: Broca's/precentral; II: postcentral/supramarginal gyrus; III: Wernicke's; IV: insular; V: other). Outcomes included extent of resection (EOR), postoperative motor/language recovery, overall survival (OS), and progression-free survival (PFS).

Results: The retrospective cohort demonstrated that AC has advantages in functional preservation across various motor/language subtypes. However, AC was associated with significantly deteriorated survival outcomes specifically in precentral gyrus GBMs. A prospective cohort study, enrolling only precentral gyrus GBMs for validation, yielded results consistent with the retrospective findings: worsened OS and PFS (OS: HR = 3.223, p = 0.0450; PFS: HR = 2.374, p = 0.0476); reduced EOR (AC: 74.3% ± 5.3%; standard craniotomy: 86.9% ± 12.3%, p = 0.0470); and better motor recovery.

Conclusions: Functional preservation and survival outcomes of AC in GBM exhibited subtype-specific correlations with tumor locations. AC with intraoperative mapping effectively preserves neurological function in GBM patients. However, for tumors involving the precentral gyrus, the AC approach carries greater risks than benefits and should be considered with caution.

Glioblastoma in adults: A Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions.

Wen PY, Weller M, Lee EQ, Touat M, Khasraw M, Rahman R, Platten M, Lim M, Winkler F, Horbinski C, Verhaak RGW, Huang RY, Ahluwalia MS, Albert NL, Tonn JC, Schiff D, Barnholtz-Sloan JS, Ostrom Q, Aldape KD, Batchelor TT, Bindra RS, Chiocca EA, Cloughesy TF, DeGroot JF, French P, Galanis E, Galldiks N, Gilbert MR, Hegi ME, Lassman AB, Le Rhun E, Mehta MP, Mellinghoff IK, Minniti G, Roth P, Sanson M Taphoorn Andreas MJB, Weiss VDT, Wick W, Zadeh G, Reardon DA, Chang SM, Short SC, van den Bent MJ, Preusser M.

Neuro Oncol. 2025 Nov 1;27(11):2751-2788. doi: 10.1093/neuonc/noaf177.

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 in 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.

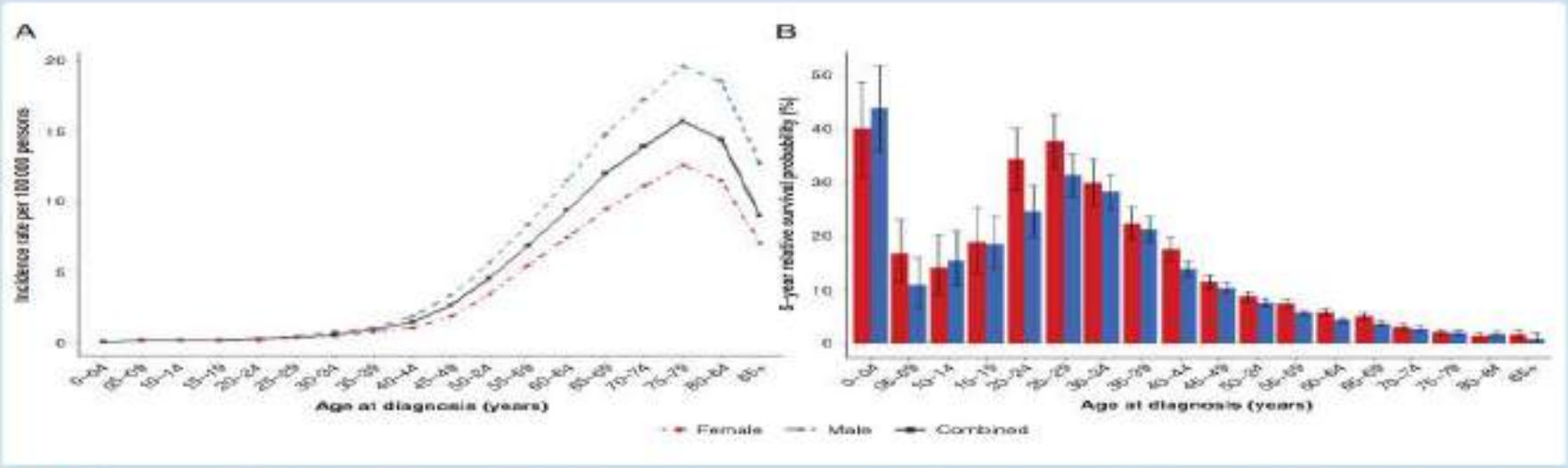


Fig. 1 Glioblastoma. (A) Incidence rate per 100 000 persons by age at diagnosis and sex, Central Brain Tumor Registry of the United States (CBTRUS) 2012–1016 (50 US states and Puerto Rico included) and (B) 5-year relative survival probability (with 95% confidence intervals) by age at diagnosis and sex, National Program of Cancer Registries (NPCR) 2012–2016 (43 US states included). **Glioblastoma defined by International

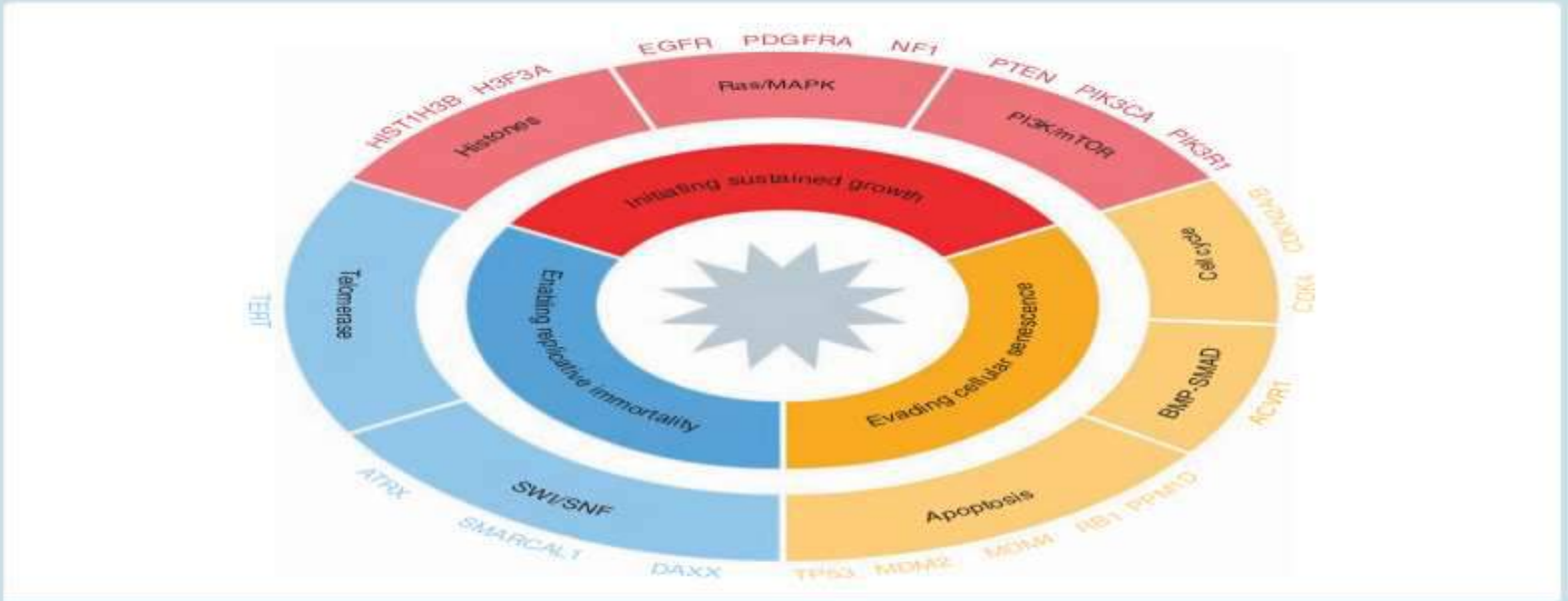
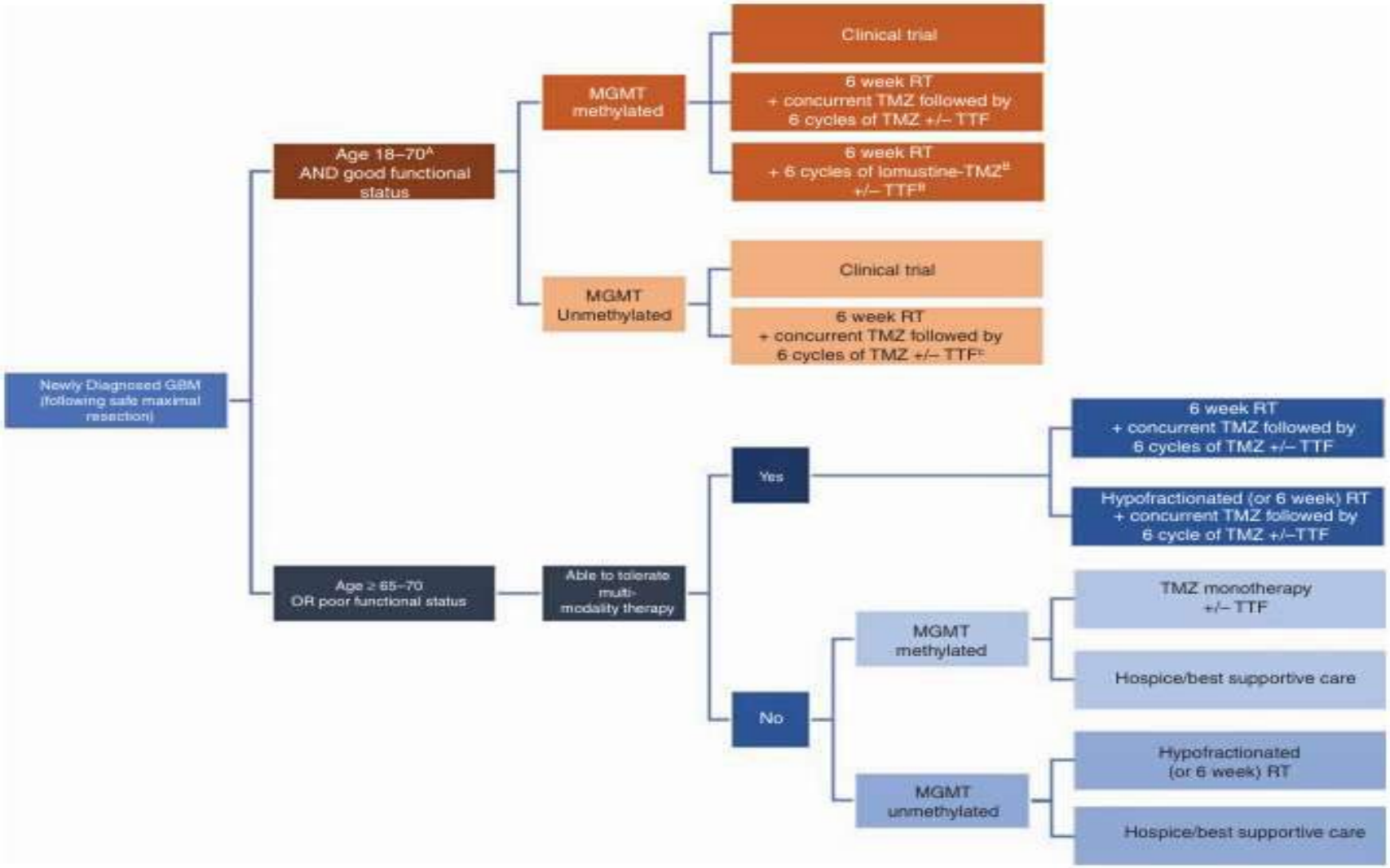


Fig. 2 Glioblastomas are characterized by somatic molecular defects in 3 major processes: initiating tumor growth, evading senescence and enabling immortal growth. Genomic abnormalities in each of the 3 processes appear required for gliomagenesis. The 3 processes are shown here, as are some of the most frequently altered genes and pathways.

Table 1 Inherited syndromes associated with adult gliomas (and adult glioblastomas) (adapted from Ostrom et al[3])

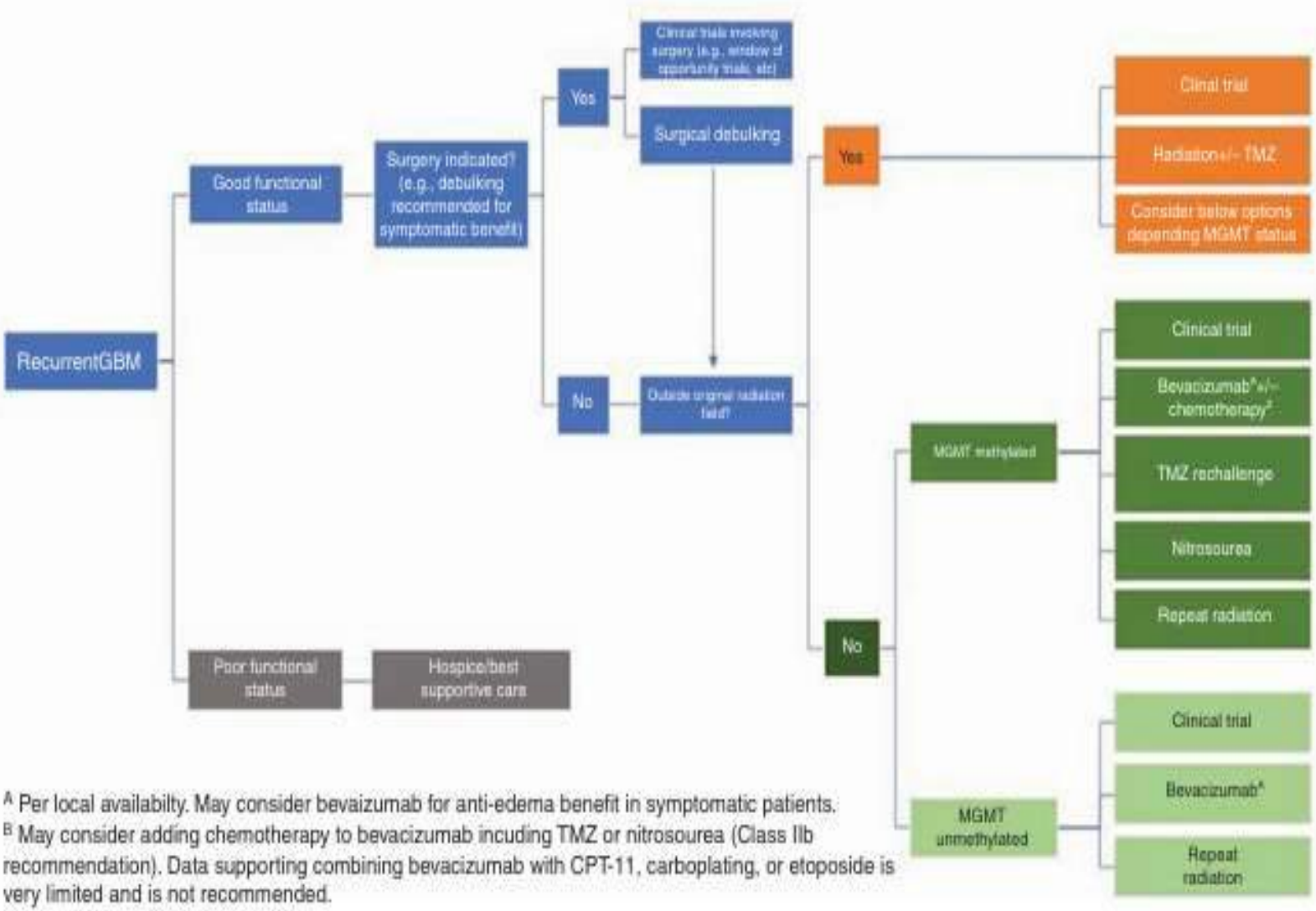
Gene Symbol (Chromosome Location)	Disorder/Syndrome (OMIM ID)	Mode of Inheritance	Phenotypic Features	Associated Brain Tumors
APC, MMR (5q21)	Familial adenomatous polyposis (FAP, 175100), Turcots syndrome type 2	Dominant	Development of multiple adenomatous colon polyps (>100), predisposition to colorectal cancer, and brain tumors	Medulloblastoma, glioma
ATM (11q22.3)	Ataxia- telangiectasia (208900)	Autosomal recessive trait	Progressive cerebellar ataxia, susceptibility to infections, predisposition to lymphoma and lymphocytic leukemia.	Astrocytoma and medulloblastoma
CDKN2A (9p21.3)	Melanoma-neural system tumor syndrome (155755)	Dominant	Predisposition to malignant melanoma and malignant brain tumors	Glioma
IDH1/IDH2 (2q33.3/15q26.1)	Ollier disease	Acquired post-zygotic mosaicism, dominant with reduced penetrance	Development of intraosseous benign cartilaginous tumors, cancer predisposition	Glioma
MLH1, PMS2	Turcots syndrome type 1	Autosomal recessive trait	Development of multiple adenomatous colon polyps (<100), predisposition to colorectal cancer, and brain tumors	Medulloblastoma, glioma,
MSH2,MLH1,MSH6,PMS2	Lynch syndrome (120435), biallelic mismatch repair deficiency, constitutional MMR *deficiency*	Dominant	Predisposition to gastrointestinal, endometrial and other cancers	Glioblastoma, other gliomas
MSH2,MLH1,MSH6,PMS2	Mismatch repair deficiency syndrome (276300)	Recessive	Pediatric cancer predisposition; café-au-lait spots; colon polyps	Glioma
NF1 (17q11.2)	Neurofibromatosis 1 (NF1) (162200)	Dominant	Neurofibromas, schwannomas, café-au-lait macules	Astrocytoma, schwannomas, optic nerve glioma
RB1 (13q14)	Retinoblastoma	Dominant	Development of multiple tumors of the eye, increased risk of some brain tumors	Retinoblastoma, pineoblastoma, malignant glioma
TP53 (17p13.1)	Li–Fraumeni syndrome (151623)	Dominant	Predisposition to numerous cancers, especially breast, brain, and soft-tissue sarcoma	Glioblastoma, other gliomas
TSC1,TSC2 (9q34.14,16p13.3)	Tuberous sclerosis (TSC) (191100, 613254)	Dominant	Development of multisystem nonmalignant tumors	Giant cell astrocytoma

Abbreviations used: ATM, ataxia telangiectasia; APC, adenomatous polyposis coli; CDKN2A, cyclin-dependent kinase inhibitor 2A; MLH1, MutL homolog 1, colon cancer, nonpolyposis type 2; MSH2, MutS protein homolog 2; MSH6, MutS protein homolog 6; OMIM, Online Mendelian Inheritance in Man; PMS2, postmeiotic segregation increased homolog 2; RB1, retinoblastoma transcriptional corepressor 1; TP53, tumor protein p53.



[A] In elderly patients with good performance status, standard 6-week radiation + TMZ can be considered
[B] It is unclear whether lomustine-TMZ is preferred over TMZ given the limitation of the study (see text.)
[C] Because MGMT methylation status is predictive of the efficacy TMZ, TMZ can be withheld in select patients with MGMT unmethylated tumors, especially in the context of cinical trials or when the risks of TMZ outweigh the benefit.

Fig. 6 Standard of care treatment paradigm for newly diagnosed glioblastoma.



[A] Per local availabilty. May consider bevaizumab for anti-edema benefit in symptomatic patients.
[B] May consider adding chemotherapy to bevacizumab incuding TMZ or nitrosourea (Class IIb recommendation). Data supporting combining bevacizumab with CPT-11, carboplating, or etoposide is very limited and is not recommended.
[C] The optimal treatment-free interval prior to pursuing TMZ rechallenge is unknown.

Fig. 7 Standard of care treatment paradigm for recurrent glioblastoma.

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

Chen D, Le SB, Ghiaseddin AP, Manektalia H, Li M, O'Dell A, Rahman M, Tran DD.

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

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.

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Efficacy and safety of immune checkpoint inhibitors and mTOR inhibitors as targeted therapy for **glioblastoma**: A systematic review and meta-analysis of randomized **clinical trials**.

Gómez EG, Morales MAM, San-Juan D, Romero-Valencia J, Mendez DLR, Hernandez DOL, Pizarro MM, Narvaez ERB, Pelayo-Salazar ME, Jimenez SM.

Neurosurg Rev. 2026 Jan 3;49(1):95. doi: 10.1007/s10143-025-04043-6.

Glioblastoma (GB) is the most common and aggressive malignant brain tumor in adults, with poor long-term survival despite standard treatment. Targeted therapies such as immune checkpoint inhibitors (ICIs) and mTOR inhibitors have been explored to improve outcomes, but their clinical benefit in GBM remains unclear. We conducted a systematic review and meta-analysis of randomized clinical trials (RCTs) evaluating the efficacy and safety of ICIs and mTORi in adult patients with newly diagnosed or recurrent GB. Databases searched included PubMed, Cochrane Library, and Semantic Scholar through March 2025. Hazard ratios (HRs) for overall survival (OS) and progression-free survival (PFS) were extracted or estimated and pooled using a fixed-effect model. Risk of bias was assessed with the Cochrane tool. Twenty-one trials involving 2,130 patients were included (12 on ICIs, 9 on mTOR inhibitors). ICIs showed no significant OS benefit (HR: 1.10; 95% CI: 0.98-1.24; p = 0.10), but a modest improvement in PFS (HR: 1.17; 95% CI: 1.04-1.33; p = 0.01). Pembrolizumab in a neoadjuvant setting demonstrated the most favorable outcomes. In contrast, mTOR inhibitors were associated with significantly worse OS (HR: 1.43; 95% CI: 1.08-1.89; p = 0.01), and no PFS benefit (HR: 1.16; 95% CI: 0.89-1.51). ICIs were commonly associated with immune-related adverse events, while mTOR inhibitors showed hematologic and metabolic toxicities. Neither ICIs nor mTOR inhibitors consistently improved survival in unselected GB populations. However, tailored approaches based on molecular features or delivery methods may offer benefits and should be further investigated.

Dual Immune Check Point Blockade in MGMT-Unmethylated Newly Diagnosed **Glioblastoma**: NRG Oncology BN007, a Randomized Phase II/III **Clinical Trial**.

Lassman AB, Polley MC, Iwamoto FM, Sloan AE, Wang TJC, Aldape KD, Wefel JS, Gondi V, Gutierrez AN, Manasawala MH, Gilbert MR, Sulman EP, Wolchok JD, Green RM, Neil EC, Lukas RV, Goldlust SA, Snuderl M, Galbraith K, Dignam JJ, Won M, Mehta MP.

J Clin Oncol. 2025 Sep 20;43(27):3032-3040. doi: 10.1200/JCO-25-00618. Epub 2025 Aug 8.

Purpose: New therapies for glioblastoma are needed, especially *MGMT*-unmethylated (u*MGMT*) disease. NRG Oncology BN002 (phase I) demonstrated safety and suggested efficacy of ipilimumab (ipi) with nivolumab (nivo) in newly diagnosed glioblastoma, leading to this phase II/III trial.

Methods: Adults with newly diagnosed u*MGMT* glioblastoma and Karnofsky performance status (KPS) ≥70 were randomly assigned to radiotherapy with either immunotherapy (ipi and nivo) or temozolomide (TMZ), stratified by recursive partitioning analysis (RPA) class and intention to use tumor treating fields. With 95% power to detect a hazard ratio (HR) ≤0.58 for progression-free survival (PFS) at a one-sided significance level (*P*) of .15, superior PFS with immunotherapy in phase II would lead to phase III overall survival (OS) testing. Corticosteroids were disallowed when starting immunotherapy. Diagnosis, biomarkers, and PFS were centrally assessed.

Results: One hundred fifty-nine participants were randomly assigned (79 immunotherapy and 80 TMZ). Arms were well balanced for age (median 60 years, range, 28-79), sex (male n = 105, 66%), KPS (90-100 n = 97, 61%), resection extent (gross total, n = 103, 65%), and RPA class (III, n = 16, 10%; IV, n = 116, 73%; V, n = 27, 17%). A preplanned analysis of phase II data conducted after 100 centrally determined PFS events showed no significant PFS improvement for ipi and nivo versus TMZ (median 7.7 months *v* 8.5 months, HR, 1.47 [70% CI, 1.19 to 1.83]; one-sided *P* = .96 [95% CI, 0.98 to 2.2]). OS is immature (>50% alive) but with no observed difference between arms (median approximately 13 months each, HR, 0.95 [95% CI, 0.61 to 1.49]; *P* = .36).

Conclusion: Ipi and nivo did not improve PFS among patients with newly diagnosed u*MGMT* glioblastoma versus TMZ. Accrual closed permanently; the trial will not proceed to phase III. No new safety signals were identified. Molecular correlative analyses and survival follow-up are ongoing.

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Angiogenesis inhibitors effects on overall survival and progression-free survival in newly diagnosed primary **glioblastoma** multiforme: a meta-analysis of twelve randomized **clinical trials**.

Motamed-Sanaye A, Mortezaei A, Afshari AR, Saadatian Z, Faraji AH, Sheehan JP, Mokhtari AM.

J Neurooncol. 2025 Jan;171(2):313-328. doi: 10.1007/s11060-024-04865-2. Epub 2024 Dec 5.

Background: Glioblastoma multiforme (GBM) is the most common malignant brain tumor in adults. Typically treated with initial surgical resection, and chemoradiotherapy, despite current treatments, patients typically survive only 12-14 months, necessitating new therapeutic approaches. Our meta-analysis evaluates combining antiangiogenic medications with chemoradiotherapy versus using chemoradiotherapy alone in treating newly diagnosed GBM.

Methods: A comprehensive literature search was conducted using PubMed/MEDLINE, Scopus, Cochrane and the Web of Science databases. The search aimed to identify studies reporting overall survival (OS), progression-free survival (PFS), and hazard ratio (HR) with corresponding confidence intervals (CIs) in patients with newly diagnosed GBM. We employed random-effect meta-analysis.

Results: Twelve randomized clinical trials (RCTs) involved 3,309 patients included in the study. The findings showed that angiogenesis inhibitors significantly prolonged PFS [HR 0.85, 95% CI (0.73, 0.99) p-value = 0.04], while there was no significant difference on OS [HR 1.014, 95%CI (0.89, 1.15), p-value = 0.84]. Bevacizumab (BEV) exhibited the highest [HR 0.67, 95% CI (0.56, 0.79), p-value < 0.0001] and thalidomide exhibited the lowest [HR 1.46, 95% CI (1.004, 2.1), p-value = 0.048] improvements of PFS. Meta-regression revealed that age, white race, study sample size, infection, vascular disease complications, KPS > 60, biopsy, gross and subtotal resection can significantly influenced the PFS, while only the year of publication affected OS.

Conclusions: The current study showed that improve the PFS with no significant effect on OS. Our findings may provide some evidence for decision-making regarding the utilization of angiogenesis inhibitors for the treatment of adult patients with newly diagnosed GBM.

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Molecularly matched targeted therapies plus radiotherapy in **glioblastoma**: the phase 1/2a N(2)M(2) umbrella **trial**.

Wick W, Lanz LM, Wick A, Harting I, Dettmer S, Suwala AK, Ketter R, Tabatabai G, Seliger C, Glas M, Burger MC, Timmer M, Ringel FA, Mildenberger I, Schulz-Schaeffer WJ, Winkler F, König L, Herold-Mende C, Eisenmenger A, Pfister SM, Renovanz M, Bendszus M, Sahm F, Platten M, Kessler T.

Nat Med. 2025 Oct;31(10):3534-3541. doi: 10.1038/s41591-025-03928-9. Epub 2025 Sep 5.

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 (N^2M^2), 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 N^2M^2 match prior experiences with the drugs in quality and quantity; no relevant negative interaction with the parallel radiotherapy was noted. The results of the N^2M^2 trial support further investigation of temsirolimus in addition to radiotherapy in patients with newly diagnosed glioblastoma with activated mTOR signaling. ClinicalTrials.gov registration: NCT03158389 .

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Vebreltinib for Previously Treated Astrocytoma, IDH-Mutant, Grade 4, and **Glioblastoma**, IDH Wild-Type with PTPRZ1-MET Fusion Gene: A Multicenter, Phase III Randomized, Open-Label **Trial**.

Bao Z, Xue Y, Liu Y, Li S, Wang L, Qu Y, Mou Y, Yu R, Wu J, Yao Y, Shu K, Hu G, Cai L, Li W, Qiu X, Li Y, Zhang L, Qi S, Ji Y, Ma C, Ma W, Li G, Tao R, Sun C, Chen L, Lv SQ, Liang P, Pan H, Peter WYM, Danny CTM, Mao Q, Wei X, Jiang T.

Cancer Commun (Lond). 2026 Mar 11;46:0019. doi: 10.34133/cancomm.0019. eCollection 2026.

Background: High-grade gliomas, including isocitrate dehydrogenase (*IDH*)-mutant astrocytoma and *IDH* wild-type glioblastoma, have a poor prognosis and limited treatment options. The *PTPRZ1-MET* (*ZM*) fusion gene is a potential therapeutic target. This study evaluated vebreltinib, a highly selective, adenosine-triphosphate-competitive inhibitor of the mesenchymal-epithelial transition factor (*MET*), in patients with *ZM*-fusion-positive glioma. **Methods:** In this multicenter, open-label *ZM* FUsion GENe (FUGEN) trial, patients with previously treated astrocytoma, *IDH*-mutant, grade 4, or glioblastoma, *IDH* wild-type, harboring the *ZM* fusion were randomized in a 1:1 ratio to receive vebreltinib (300 mg orally twice daily) or control treatment (temozolomide or cisplatin plus etoposide) in 28-d cycles. The primary end point was overall survival (OS). Key secondary end points included progression-free survival (PFS), objective response rate (ORR), and safety analyses. **Results:** Eighty-one patients (42 in the vebreltinib group and 39 in the control group) were included in the full analysis set. As of 2023 April 1, the median follow-up duration was 5.9 (range, 0.8 to 44.7) months in the vebreltinib group and 3.4 (range, 0.5 to 40.5) months in the control group. Median OS was significantly longer in the vebreltinib group than in the control group (6.3 months versus 3.4 months; hazard ratio [HR], 0.52; 95% confidence interval [CI], 0.32 to 0.85; stratified log-rank $P = 0.007$). In the *IDH*-mutant subgroup, median OS was 7.7 months in the vebreltinib group and 3.3 months in the control group (HR, 0.48; 95% CI, 0.28 to 0.80; stratified log-rank $P = 0.005$). Among patients with a baseline tumor diameter of ≤3.0 cm, median OS was 32.5 months in the vebreltinib group versus 4.2 months in the control group (HR, 0.27; 95% CI, 0.07 to 1.06; stratified log-rank $P = 0.046$). Median PFS was also longer in the vebreltinib group (1.9 months versus 1.1 months; HR, 0.54; 95% CI, 0.33 to 0.88; stratified log-rank $P = 0.012$). The ORR was 9.5% with vebreltinib and 2.6% with control treatment. The incidence of grade ≥3 adverse events was comparable between groups, and no treatment-related deaths were reported. **Conclusion:** Vebreltinib significantly improved OS in patients with previously treated high-grade glioma harboring the *ZM* fusion, particularly in the subgroup with *IDH*-mutant astrocytoma, and the safety profile was manageable. **Trial registration:** This study was registered with the Chinese Drug Clinical Trial Registry (ChinaDrugTrials.org.cn) under the identifier, CTR20181664 (registration date: 2018 September 19).

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Evaluation of Regorafenib in Newly Diagnosed and Recurrent **Glioblastoma**: GBM AGILE Phase II/III Bayesian Randomized Platform **Trial**.

Wen PY, Berry DA, Buxton MB, Colman H, de Groot J, Lim M, Mellinghoff I, Perry JR, Weller M, Blondin NA, Butt OH, Damek DM, de la Fuente MI, Drappatz J, Dunbar E, Giglio P, Hyddmark EV, Iwamoto F, Jaeckle KA, Kim L, Kling HM, Lee EQ, Mantica M, Mikkelsen T, Nabors B, Newton HB, Olson JJ, Schiff D, Walbert T, Weathers SP, Cloughesy T, Lassman AB; GBM AGILE Regorafenib Study Group.

J Clin Oncol. 2026 Jun 20;44(18):1676-1686. doi: 10.1200/JCO-25-01137. Epub 2026 Apr 14.

Purpose: GBM AGILE (ClinicalTrials.gov identifier: NCT03970447) is a phase II/III Bayesian adaptive platform registration trial testing multiple arms against a common control; the primary end point is overall survival (OS). Regorafenib, a multikinase inhibitor, showed OS benefit in recurrent (RD) glioblastoma in the phase II REGOMA trial and entered GBM AGILE as the first investigational arm.

Methods: Patient subtypes included in the regorafenib arm of GBM AGILE were newly diagnosed unmethylated (NDU) and RD glioblastoma. Prospective defined sets of subtypes, or arm signatures, were NDU, RD, and all (NDU + RD). As the first investigational arm in GBM AGILE, regorafenib was equally randomized to the control arm. Treatment in the control arm is temozolomide + radiotherapy (in newly diagnosed) or lomustine (in RD). Efficacy was assessed by OS hazard ratio (HR), arm/control, and demonstrated when the Bayesian probability of benefit (HR <1.00) was ≥98%. Analysis was performed monthly for limited efficacy, which occurs when the Bayesian predictive power is <25% for all signatures, and determines stopping enrollment. Follow-up continued for 12 months after accrual stopped.

Results: When the predictive power was <25% in all predefined signatures for regorafenib, accrual stopped for limited efficacy. The final analysis did not demonstrate OS improvement in the regorafenib arm in RD nor NDU glioblastoma. Median HRs were 1.05 (NDU), 1.07 (RD), and 1.07 (all) with final probabilities of benefit (HR <1.00) of 0.421 (NDU), 0.312 (RD), and 0.296 (all). Regorafenib was associated with increased toxicity relative to control.

Conclusion: GBM AGILE did not show superiority of regorafenib over control in RD (lomustine) or NDU (temozolomide + radiotherapy) glioblastoma, yet caused increased toxicities. Regorafenib has been removed from National Comprehensive Cancer Network guidelines as a treatment option for RD.

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Phase 2 study of regorafenib in patients with progressive **glioblastoma** after failure of bevacizumab.

Lucas A, Peereboom D, Rauf Y, Li H, Hanlon J, Ahluwalia M.

Neurooncol Adv. 2026 Jun 9;8(1):vdag144. doi: 10.1093/noajnl/vdag144. eCollection 2026 Jan-Dec.

Background: Treatment options in progressive glioblastoma (GBM) are limited, especially in patients who have experienced disease progression while receiving bevacizumab therapy. This phase 2 study was conducted to evaluate the efficacy and safety of regorafenib monotherapy in patients with GBM.

Methods: Eligible patients had radiographic progression of histologically confirmed GBM following second- or third-line bevacizumab therapy. They received regorafenib monotherapy using the dose escalation strategy demonstrated in the ReDOS phase 2 clinical trial evaluating regorafenib in metastatic colon cancer. The target dose was 160 mg once daily, administered for 3 weeks on/1 week off in 28-day cycles. Patients underwent brain magnetic resonance imaging (MRI) every 8 weeks and were assessed via modified Response Assessment in Neuro-Oncology criteria. Patients continued treatment with regorafenib therapy until they experienced progression or excessive toxicity.

Results: Based on the analysis of 13 enrolled patients, there were no responses and 12 of 13 (92.3%) had progressive disease on brain MRI; 1 patient went off study due to an adverse event occurring before assessment. The median overall survival (OS) was 4.1 months (95% CI 2.0-7.3). The OS at 12 months was 23% (0.2-46). The PFS at both 3 and 6 months was 7.7% (0.0-22.2%) with a median PFS of 1.0 month, (0.4-1.8). There was a total of 14 Grade 3 or 4 AEs and no Grade 5 AEs.

Conclusions: Regorafenib did not improve OS or PFS in bevacizumab-refractory recurrent glioblastoma. The study was halted early due to futility.

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

Rha SY, Castanon E, Gill S, Senellart H, Lopez J, Márquez-Rodas I, Victoria I, Kim TM, Lwin Z, Burger MC, Simonelli M, Cassier PA, Hendifar AE, Ascierto PA, Dutcus C, Okpara CE, Ghori R, Jin F, Groisberg R, Villanueva L.

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

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.

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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.**

Habibi MA, Ahmadvand MH, Delbari P, Mirjani MS, Zare AH, Mehdizadeh B, Allahdadi A, Ardestani Z, Rad RH, Aliasgary A, Sabet S, Eftekhar MS, Mohammadzadeh I, Hajikarimloo B.

J Clin Neurosci. 2025 May;135:111138. doi: 10.1016/j.jocn.2025.111138. Epub 2025 Feb 28.

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.

Combination of metronomic oral pazopanib and topotecan for recurrent **glioblastoma** with and without previous bevacizumab: Results from a phase 2 **clinical trial**.

Ozer BH, Cohen AL, Colman H, Penas-Prado M, de Groot J, Loghin ME, Pan E, Raizer JJ, Kumthekar P, F
KL, Walbert T, Merrell RT, Groves MD, Ahluwalia MS, Wu J, Burton EC, Vera E, Mendoza T, Grajkowska E
Wall K, Reyes J, Yuan Y, Armstrong TS, Gilbert MR.

Neurooncol Adv. 2026 Jan 23;8(1):vdaf261. doi: 10.1093/noajnl/vdaf261. eCollection 2026 Jan-Dec.

Background: Glioblastoma (GBM) has limited effective salvage therapy options. The combination of the Type 1B topoisomerase/HIF1α inhibitor topotecan and the tyrosine kinase inhibitor pazopanib has shown promise in solid tumors and may be effective in recurrent GBM.

Methods: Patients with recurrent GBM who were bevacizumab-naïve (Group A, 9 patients) or had previous bevacizumab (BEV) (Group B, 22 patients) started daily oral pazopanib (600 mg) and topotecan (0.25 mg). The primary objective was progression-free survival (PFS) at 6 months for Group A and 3 months for Group B patients. Secondary objectives included median progression-free and overall survival (OS), safety, tolerability, and toxicity as measured by patient-reported outcomes (PROs) and adverse event documentation.

Results: Group A enrolled 9 evaluable patients and closed to accrual early when interim primary objectives were not met (PFS-6 11%). Group B enrolled 22 evaluable patients and narrowly met its primary objective (PFS-3 18%). Median PFS and OS endpoints demonstrated equivalent to slight improvement upon historical metrics, respectively. The regimen was tolerable and safe save for high frequency of hypertension, with PROs data showing stability or worsening in parallel with tumor stability or progression, respectively.

Conclusions: These findings suggest the regimen is safe and tolerable to GBM patients. The regimen was ineffective in bevacizumab-naïve patients and only narrowly met its predetermined endpoint in patients with prior BEV. These results do not support the combination regimen as tested in this protocol for further investigation in GBM.

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Efficacy and safety of tumor treating fields (TTF) combined with chemotherapy versus chemotherapy only in the treatment of **glioblastoma**: a systematic review and meta-analysis.

Abuliezi N, Sun Y, Zhao J, Qu X, Wu Y, Liao T, Kuerban G, Dun X, Wu Q.

Front Med (Lausanne). 2026 May 8;13:1812119. doi: 10.3389/fmed.2026.1812119. eCollection 2026.

Background: This systematic review and meta-analysis aimed to evaluate the efficacy and safety of tumor treating fields (TTF) combined with chemotherapy compared with chemotherapy alone in patients with newly diagnosed and recurrent glioblastoma (GBM).

Method: A systematic search was conducted in PubMed, Embase, Web of Science, Cochrane Library, and databases from their inception to 10 December 2025. Randomized controlled trials, controlled clinical trials and observational cohort studies evaluating the efficacy and safety of TTF in GBM treatment were included. Evaluating the efficacy and safety of TTF in GBM treatment were included. Data were pooled using Stata 15 software.

Results: A total of 14 studies involving 2,376 patients (both newly diagnosed and recurrent GBM) were included: 7 RCTs, 4 CCTs, and 3 observational cohort studies were included. Pooled analyses demonstrated that compared with chemotherapy alone, TTF combined with chemotherapy significantly prolonged progression-free survival (PFS) (HR = 0.62, 95% CI: 0.55-0.69, $P < 0.0001$) and overall survival (OS) (HR = 0.63, 95% CI: 0.56-0.72, $P < 0.0001$) in both newly diagnosed and recurrent GBM patients. No significant difference in systemic adverse events was observed between the two groups (OR = 1.10, 95% CI: 0.79-1.53, $P = 0.571$); however, the incidence of skin irritation was significantly higher in the TTF group (OR = 12.87, 95% CI: 7.47-22.18, $P < 0.0001$). Subgroup analyses indicated that patient diagnosis type contributed to heterogeneity across studies.

Conclusion: In newly diagnosed and recurrent GBM, TTF combined with chemotherapy significantly improves survival outcomes compared with chemotherapy alone, highlighting the therapeutic value and safety of the combined treatment in both patient populations.

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

Iwamoto FM, Tanguturi SK, Nayak L, Wang TJ, Desai A, Lustig RA, Bagley S, Wong ET, Hertan LM, McCluskey C, Hayden J, Muzikansky A, Nakhawa S, Japo J, Bossi CC, Meylan M, Tian Y, Barlow GL, Speliakos P, Ayoub G, Meredith DM, Ligon KL, Haas-Kogan D, Huang K, Wucherpfennig KW, Wen PY, Reardon DA.

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

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.

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Dose escalation with intraoperative radiotherapy in newly diagnosed **glioblastoma** (INTRAGO-II): an open-label, multicentre, randomised, controlled, phase 3 **trial**.

Giordano FA, Ganslandt O, Münter MW, Combs SE, Diehl C, Meyer B, Herrlinger U, Schneider M, Kahl KH, Shiban E, Goenka A, Schulder M, Lucas A, Plans G, Brehmer S, Ruder AM, García-Cabezas S, Solivera J, Cifarelli CP, Wenz F, Sarria GR, Pope WB, Layer JP, Tsien CI, Petrecca K; INTRAGO-II Study Group.

Lancet Oncol. 2026 Jul;27(7):864-878. doi: 10.1016/S1470-2045(26)00235-4.

Background: Despite maximal safe resection and chemoradiotherapy, most glioblastomas recur locally. We aimed to evaluate whether additional intraoperative radiotherapy compared with standard of care improves outcomes in patients with newly diagnosed glioblastoma.

Methods: INTRAGO-II was an open-label, multicentre, randomised, controlled, phase 3 trial enrolling patients aged 18-80 years with supratentorial glioblastoma amenable to resection of the contrast enhancing tumour with Karnofsky performance score (KPS) of ≥60%. Patients from 18 centres in Brazil, Canada, China, Germany, Spain, South Korea, and the USA were randomly assigned (1:1) intraoperatively to receive additional kilovoltage intraoperative radiotherapy with 30 Gy (intraoperative radiotherapy group) or surgery alone (standard-of-care group), stratified by age, KPS, and residual tumour. Postoperative treatment consisted of external-beam radiotherapy to 60 Gy with concurrent temozolomide (75 mg/m^2), followed by six adjuvant cycles of temozolomide (150-200 mg/m^2, days 1-5 every 28 days). The primary endpoint was median progression-free survival in the full-analysis set, confirmed by masked, centralised review. This ongoing study is closed to recruitment and is registered with ClinicalTrials.gov, NCT02685605.

Findings: Between Dec 9, 2016, and June 17, 2024, of 411 patients assessed for eligibility, 314 were randomly assigned. The full-analysis set comprised 298 patients (intraoperative radiotherapy, n=161; standard-of-care, n=137), of whom 127 (43%) patients were female and 171 (57%) were male. Data on race and ethnicity were not collected. At a median follow-up of 17·2 months (IQR 10·5-27·1), median progression-free survival was 11·0 months (95% CI 9·2-12·6) in the intraoperative radiotherapy group versus 11·4 months (9·7-13·9) in the standard-of-care group (hazard ratio [HR] 1·1, 95% CI 0·85-1·44; p=0·47). Local recurrence was the predominant pattern of failure in both groups (76 [72%] in the intraoperative radiotherapy group vs 60 [71%] in the standard-of-care group, p=0·87). The most common grade 3-4 adverse events were seizure (21 [13%] in the intraoperative radiotherapy group vs nine [7%] in the standard-of-care group), radiation necrosis (11 [7%] vs three [2%]; p=0·06), thrombocytopenia (seven [4%] vs 11 [8%]), and muscle weakness (12 [7%] vs 19 [14%]). In total, 252 serious adverse events occurred in 105 (65%) patients in the intraoperative radiotherapy group and 142 serious adverse events in 72 (53%) patients in the standard-of-care group. Of these, 65 (26%) events in 40 (38%) patients in the intraoperative radiotherapy group and 27 (19%) events in 19 (26%) patients in the standard-of-care group were considered possibly related to the treatment. Of all grade five adverse events reported, 14 in the intraoperative radiotherapy group (CNS toxicity [n=2], myocardial infarction [n=2], sepsis [n=2], and one each cardiac arrest, fever, lung infection, fracture, postoperative haemorrhage, neoplasm, haematoma, and not otherwise specified death) and six in the standard-of-care group (lung infection [n=2], and one each multiorgan failure, encephalitis, neoplasm, and cystitis) were attributable to specific CTCAE terms.

Interpretation: Instant, spatially precise dose escalation with intraoperative radiotherapy added to standard of care did not improve outcomes, questioning the value of further local dose intensification in resectable glioblastoma.

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Low-Dose Fractionated Radiation Therapy as a Chemopotentiator of Temozolomide for Recurrent Anaplastic Astrocytoma and **Glioblastoma**: A Single-Arm Phase 1/2 **Trial**.

Lin T, Ke S, Hu C, Assadi R, Huang J, Gupta S, Rawojc K, Kleinberg L, Mukherjee D, Rincon-Torroella J, Weingart JD, Holdhoff M, Grossman S, Ahmed MM, Redmond KJ.

Int J Radiat Oncol Biol Phys. 2026 Mar 15;124(4):1003-1014. doi: 10.1016/j.ijrobp.2025.10.014. Epub 2025 Oct 24.

Purpose: Preclinical and clinical studies suggest low-dose fractionated radiation therapy (LDFRT) is a chemopotentiator in several solid tumors. We evaluated chemopotentiation of temozolomide with LDFRT in glioblastoma and brain metastatic lung cancer cell lines, followed by a phase 1/2 trial assessing the safety/efficacy of LDFRT with concurrent/adjuvant temozolomide in patients with recurrent high-grade gliomas (HGGs).

Methods and materials: Preclinical-The temozolomide-potentiating effect of LDFRT was tested in glioblastoma and brain metastatic lung cancer cell lines with real-time cell electronic sensing system and flow cytometry. Clinical-Patients with recurrent HGG following standard-of-care chemoradiation therapy and adjuvant temozolomide were enrolled. Radiation therapy consisted of 0.5 Gy twice daily fractions with concurrent temozolomide on days 1 to 5 of a 28-day cycle for 6 cycles, and adjuvant temozolomide for 6 cycles. Magnetic resonance imaging was performed every 2 months after initiating LDFRT. The phase 1 primary endpoint was acute hematologic toxicity. The phase 2 primary endpoint was 1-year overall survival (OS), with a lower bound of 80% confidence interval > 28.6% (historical control). Secondary endpoints included pseudoprogression incidence.

Results: Preclinical-LDFRT-mediated temozolomide potentiation appears more effective than 2 Gy-mediated potentiation. Clinical-Thirty patients were enrolled from 2013 to 2021; 80% had recurrent glioblastoma and 90% were Eastern Cooperative Oncology Group 0-1. Among patients with molecular data, 61% were O-6-methylguanine-DNA methyltransferase-methylated and 23% were isocitrate dehydrogenase-mutant. Median RT dose was 30 Gy (range, 28.5-30 Gy). Median follow-up was 9.5 months (range, 0.1-66.3 months). One-year OS was 34.5% (95% confidence interval [CI], 20.9-57.0; lower bound of 80% CI = 24.8%). 77% experienced pseudoprogression (median dose 10 Gy; range, 6-30 Gy), corresponding with improved OS (HR, 0.12; 95% CI, 0.03-0.40; P < .01) versus no pseudoprogression.

Conclusions: Preclinical work demonstrates the chemopotentiating effect of LDFRT. In our clinical trial, LDFRT with temozolomide was safe and well tolerated in patients with recurrent HGG receiving salvage reirradiation. Although the primary survival endpoint was not achieved, high pseudoprogression rates at low radiation doses support the principle of low-dose radiation hypersensitivity mediated by chemopotentiation and potentially immune-modulation.

Ultra-hypofractionated versus conventional chemoradiation for newly diagnosed **glioblastoma**: Survival and toxicity results of a multicenter randomized **trial**.

de Jong AM, van der Boog ATJ, Wester G, Eekers DBP, Budiharto TCG, Rozema T, Lagerwaard FJ, Bruynzeel AME, de Groot C, van der Meulen M, Cialdella F, Dankbaar JW, Hendrikse J, Kleynen KE, Claes A, Philippens MEP, Smid EJ, de Vos FYFL, van Rossum PSN, Robe PA, David S, Snijders TJ, Verhoeff JJC.

Radiother Oncol. 2026 Oct;223:111726. doi: 10.1016/j.radonc.2026.111726. Epub 2026 Aug 8.

Purpose: In glioblastoma, standard first-line chemoradiation since the 2005 EORTC/NCIC trial is 30x2Gy with concurrent and adjuvant temozolomide. A phase II study suggested ultra-hypofractionation (6x6Gy) may offer comparable survival, with reduced treatment time and costs, potentially improving health-related quality of life (HRQoL). This phase III randomized trial (Netherlands Trial Registry, NL72953.041.20) evaluated non-inferiority of ultra-hypofractionated temozolomide chemoradiation in glioblastoma patients.

Patients and methods: Adults with newly diagnosed glioblastoma and a Karnofsky performance status ≥70 were randomized (1:1) to ultra-hypofractionated (6x6Gy in 2 weeks) or standard (30x2Gy in 6 weeks) radiotherapy, both with concurrent and 6 cycles of adjuvant temozolomide. The primary endpoint was 2-year overall survival (OS); the non-inferiority margin was a hazard ratio of 1.2. Secondary outcomes included progression-free survival (PFS) and toxicity.

Results: Enrollment stopped early, due to slow accrual (n=135/474 planned, 67 experimental, 68 standard). Median OS was shorter in the experimental arm: 13.0 months (95% CI 10.3-15.7) versus 21.0 months (95% CI not estimable). In a time-dependent analysis, survival was similar in the first 6 months (HR 0.99, 95% CI 0.39-2.50), but mortality was higher thereafter (HR 2.54, 95% CI 1.57-4.09, p < 0.001). Radiation necrosis or pseudoprogression was more frequent after ultra-hypofractionation (47.8% vs 16.2%; HR 5.20, 95% CI 2.56-10.58), with increased dexamethasone use at 6-12 months. No grade 4-5 toxicities were observed.

Conclusion: Non-inferiority of the 6x6 Gy chemoradiation regimen could not be demonstrated. This ultra-hypofractionated regimen was associated with inferior survival and increased radiation necrosis, and therefore should not replace standard chemoradiation.

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

Brown NF, McBain C, Brazil L, Peoples S, Jefferies S, Harris F, Vinayan A, Plaha P, Brooks C, Hussain S, Dutton SJ, Cook J, Ng SM, Levy S, Coutts T, Mulholland P.

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

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.

Proton Pump Inhibitor Use and Survival in Patients With Newly Diagnosed **Glioblastoma.**

Le Rhun E, Sain D, Erridge SC, Reardon DA, Minniti G, Roth P, Wick W, Nabors B, Sampson J, Mason W, Cloughesy T, Reijneveld JC, Stupp R, Preusser M, Gorlia T, Weller M.

JAMA Netw Open. 2025 Nov 3;8(11):e2545578. doi: 10.1001/jamanetworkopen.2025.45578.

Importance: Proton pump inhibitors (PPI) are often prescribed to prevent steroid-induced gastritis and peptic ulcer disease in patients with glioblastoma. Yet, these drugs may enhance the activity of aldehyde dehydrogenase 1 A1 (ALDH1A1), which has been linked to protection from oxidative stress, radiotherapy, and chemotherapy.

Objective: To explore the associations of the use of potent ALDH1A1-activating PPIs (PA-PPIs) and other antacid drugs with outcomes in patients with newly diagnosed glioblastoma.

Design, setting, and participants: This meta-analysis was a secondary analysis of individual prospectively captured patient data using a dataset of 5 randomized clinical trials conducted between 2008 and 2020. Participants included patients with a new diagnosis of glioblastoma. Data analysis was completed in November 2024.

Exposure: We assessed drug use at baseline and defined 3 landmarks: start of temozolomide maintenance cycles 1 (landmark 1) and 4 (landmark 2), and end of cycle 6 (landmark 3).

Main outcomes and measures: The primary outcome measures were progression-free survival (PFS) and overall survival (OS) from baseline and from the start of each corresponding landmark time.

Results: The study population included 2981 patients (1858 [62.3%] male; median [range] age, 58 [18-85] years). On univariate analysis, patients treated with PA-PPI had worse PFS and OS at all 4 time points. The multivariate analysis accounting for age, sex, performance status, steroid use, extent of resection, and MGMT status confirmed a difference for PFS at landmarks 1 (hazard ratio [HR], 1.14 [95% CI, 1.01-1.28]), 2 (HR, 1.26 [95% CI, 1.09-1.44]), and 3 (HR, 1.31 [95% CI, 1.10-1.56]), and for OS at landmarks 1 (HR, 1.34 [95% CI, 1.08-1.66]) and 2 (HR, 1.14 [95% CI, 1.01-1.29]). No such association was seen for the use of other antacid drugs. The negative association of PA-PPI use with PFS and OS was observed independently of MGMT promoter methylation and steroid use.

Conclusions and relevance: In this meta-analysis of patients with newly diagnosed glioblastoma, PPI use was associated with inferior survival outcomes. These findings suggest that PA-PPI use should be discouraged in patients with glioblastoma, since alternative agents are available and a detrimental effect cannot be excluded. Translational research studies should explore whether PPI-induced activity of ALDH mediates the potential adverse effects of PPI in glioblastoma. .

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Impact of nurse navigation and mobile app on brain tumor patients receiving oral anticancer therapy.

Poisson C, Duflot-Boukobza A, Mathivon D, Khettab M, Ferrua M, Fourcade A, Lezghed N, Dhermain F, Lemare F, Puglisi V, Abbas M, Di Palma M, Scotté F, Minvielle E, Mir O, Guyon D, Dumont SN.

NPJ Digit Med. 2026 Jan 15;9(1):143. doi: 10.1038/s41746-025-02325-3.

Oral anticancer agents (OAAs) are commonly prescribed for patients with primary brain tumors, but adherence can be challenging due to cognitive impairment and discontinuous treatment schedules. This subgroup analysis of the randomized phase 3 CAPRI trial evaluated the impact of a nurse navigator-led intervention combined with a digital platform (web portal and mobile app) versus standard care in patients with primary brain tumors treated with OAAs. The primary endpoint was Relative Dose Intensity (RDI), with secondary endpoints including adherence, toxicity, healthcare utilization, and patient-reported experience. Fifty-one patients were included between October 2016 and May 2019, 63% of whom had glioblastoma. Twenty-six patients received the intervention. RDI wa significantly higher in the intervention group compared to the control group (105% ± 12 vs. 97.6% ± 13, p = 0.04). The intervention also resulted in fewer emergency room visits, reduced hospitalizations, greater use of supportive care services, and improved patient-reported experience (all p < 0.05). Remote monitoring allowed early corticosteroid adjustments in cases suggestive of intracranial hypertension, helping to prevent hospitalizations. No significant differences were observed in treatment-related toxicity. These findings suggest that a nurse navigator-led digital intervention can improve care continuity and outcomes in this population and merit further investigation.

Early onset radiation-induced leukoencephalopathy in patients treated for a **glioblastoma** by STUPP protocol and risk factors evaluation, an ancillary study of the phase III ASTER protocol.

Balcerac A, Cuzzubbo S, Bompaire F, Ducray F, Kremer S, Sanson M, Psimaras D, Vicaut E, Carpentier AF, Ricard D.

Rev Neurol (Paris). 2026 Mar;182(3):186-192. doi: 10.1016/j.neurol.2026.01.005. Epub 2026 Feb 4.

Background: Since 2005, the standard treatment for newly diagnosed glioblastoma involves radiotherapy combined with concomitant and adjuvant temozolomide (TMZ), as per the Stupp protocol. A known long-term complication of radiotherapy is Radiation-Induced Leukoencephalopathy (RIL), characterized by diffuse FLAIR-hyperintensities and cortico-subcortical brain atrophy, often leading to cognitive, balance and urinary impairments. While RIL has been typically described years after treatment in long survivors, there is little information regarding early-onset RIL (<6 months) and its potential risk factors.

Objective: This ancillary study aims to assess the incidence of early-onset RIL in glioblastoma patients treated within the ASTER phase III trial. Additionally, we explored potential risk factors, including genetic susceptibility, and evaluate whether Losartan, a PPARγ agonist, reduces early RIL incidence.

Methods: We conducted a retrospective analysis of data from the ASTER trial, a randomized, placebo-controlled phase III study evaluating the effects of Losartan on corticosteroid needs in glioblastoma patients receiving standard radiotherapy with concomitant TMZ. Patients were included if they had MRI scans available at baseline and six months post-treatment, with no evidence of tumor progression. Early-onset RIL was defined as an increase of at least two points on the simplified Scheltens rating scale, with associated cortical-subcortical atrophy. Genetic testing focused on the PPARγ germline SNP rs2120825. Statistical analyses included univariate comparisons of clinical and genetic variables.

Results: Among the 31 patients included, 29% (n=9) developed early-onset RIL. No significant associations were found between early RIL and known risk factors such as smoking (P=0.43), hypertension (P=0.12), age (P=0.067), or PPARγ TG polymorphism (P=0.68). Similarly, Losartan administration (100mg/day) showed no significant effect on prevention of early RIL (P=0.72). The limited power of the study may explain the lack of significant findings.

Conclusion: This study reports a high incidence (29%) of early-onset RIL in glioblastoma patients treated with the Stupp protocol, highlighting the question of individual sensitivity to this severe side effect. While previous research suggests a role for PPARγ in radiation-induced toxicity, this study was underpowered to confirm whether Losartan, as PPARγ agonist, could offer protection against early-onset RIL. The lack of significant results underscores the need for larger, prospective trials to further investigate these factors and develop targeted preventive strategies.

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Nomograms for predicting survival of elderly patients with newly diagnosed **glioblastoma**: a secondary analysis of the CCTG CE.6 **trial**.

Moraes FY, Isen J, Perry J, Laperriere N, Brandes AA, Menten J, Phillips C, Fay M, Nishikawa R, Mason WP, Cairncross JG, Roa W, Ding K, O'Callaghan C.

J Neurooncol. 2026 Jan 19;176(3):171. doi: 10.1007/s11060-025-05399-x.

BACKGROUND: Glioblastoma (GB) in the elderly is associated with poor prognosis and outcome heterogeneity. We aimed to develop and validate prognostic nomograms for elderly GB patients using data from the CCTG CE.6 trial. METHODS: Data from 562 patients (≥ 65 years) randomized to radiotherapy alone (RT) or radiotherapy plus temozolomide (RT + TMZ) were divided into training and testing cohorts (3:2 ratio). Cox regression identified prognostic factors associated with overall survival (OS), which were integrated into multivariable models. Nomograms were constructed, internally validated, and used to stratify patients into risk groups. Kaplan–Meier survival estimates and log-rank tests assessed model performance. RESULTS: In the RT + TMZ cohort, low MMSE, biopsy-only resection, male sex, and MGMT status unknown were independently associated with poorer OS. Median OS in training data was 5.7, 10.9, and 13.8 months for high-, middle-, and low-risk groups, respectively, with comparable results in validation (6.6, 9.9, and 13.1 months). PFS stratification also showed significant differences (median 3.3, 6.0, and 7.6 months). For the RT-alone arm, biopsy-only resection and male sex were prognostic, with risk groups demonstrating significant OS and PFS differences. CONCLUSIONS: Trial-based nomograms were developed and validated for elderly GB patients, effectively stratifying risk and predicting survival. These tools may guide individualized prognostication, inform treatment decisions, and improve trial design in this underrepresented population.

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

Fleming JL, Pugh SL, Chang SM, McElroy JP, Becker AP, Aldape KD, Shih HA, Ashby LS, Hunter GK, Bahary JP, Schultz CJ, Kavanagh BD, Puduvalli VK, Robins HI, Werner-Wasik M, Mehta M, Chakravarti A.

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.

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.

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Expedited chemoradiation after laser interstitial thermal therapy (LITT) is feasible and safe in patients with newly diagnosed **glioblastoma**.

Yu JS, Meade SM, Zhao R, Wei W, Dashora H, Prayson R, Grabowski MM, Stevens G, Lobbous M, Murphy ES, Suh JH, Chao ST, Barnett GH, Peereboom D, Ahluwalia MS, Mohammadi AM.

Neurooncol Adv. 2025 Feb 14;7(1):vdaf038. doi: 10.1093/noajnl/vdaf038. eCollection 2025 Jan-Dec.

Background: High-grade gliomas (HGG) are incurable primary brain tumors. Laser interstitial thermal therapy (LITT) has emerged as an alternative to surgery for select patients. Hyperthermia can improve the efficacy of radiation and chemotherapy. Shortening the time between LITT and chemoradiation may maximize their biological and clinical benefits. This trial evaluated the safety and feasibility of expediting chemoradiation after biopsy and LITT in patients with newly diagnosed HGG.

Methods: Patients with suspected HGG were enrolled. Those with pathologic confirmation of HGG and deemed appropriate candidates for LITT and chemoradiation were considered evaluable. Participants underwent 6 weeks of adjuvant chemoradiation initiated within 7 days of LITT. Endpoints were assessed until the completion of radiation and included the occurrence of wound dehiscence; new, treatment-refractory seizures; cerebral edema; and completion of planned radiotherapy.

Results: Thirteen patients with suspected HGG were enrolled, and ten were considered evaluable. All 10 patients were diagnosed with glioblastoma (GBM, IDHwt). Three patients were deemed unevaluable: 2 patients with other CNS tumors and one GBM patient who developed grade 4 postoperative edema. Of 10 evaluable patients, the median age was 60.2 years (IQR: 51.0, 69.4), and median preoperative KPS was 90 (IQR: 90, 80). The median time between LITT and the initiation of chemoradiation was 7 days. There were no occurrences of significant protocol-related adverse events.

Conclusions: Accelerated initiation of chemoradiation after biopsy and LITT is safe and feasible for patients with newly diagnosed GBM. A larger study is needed to assess potential synergy of hyperthermia and chemoradiation to improve survival.

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

Yeboa DN, Braunstein SE, Cabrera A, Crago K, Galanis E, Hattab EM, Heron DE, Huang J, Kim MM, Kirkpatrick JP, Knisely JPS, McAleer MF, McClelland S 3rd, Milano MT, Moliterno J, Porter A, Redmond KJ, Trifiletti DM, Tsien C, Venkatesulu BP, Vinogradskiy Y, Bradfield L, Helms AR, Bovi JA.

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

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.

MRI-guided adaptive radiotherapy for high **grade glioma** (UNITED): a single-centre, single-arm, non-inferiority, phase 2 **trial**.

Detsky JS, Chan AW, Moore-Palhares D, Safavi AH, Perry J, Fat MJL, Atenafu EG, Das S, Lipsman N, Heyn C, Maralani P, Czarnota GJ, Ruschin M, Keller B, Lau A, Chen H, Myrehaug SD, Soliman H, Tseng CL, Sahgal A.

Lancet Oncol. 2026 Jun;27(6):729-737. doi: 10.1016/S1470-2045(26)00088-4. Epub 2026 May 14.

Background: Radiotherapy volumes for patients with glioblastoma have remained unchanged for decades and result in large volumes of irradiated brain. We aimed to show the safety of a small-margin, MRI-guided adaptive radiotherapy approach for glioblastoma.

Methods: This single-arm, phase 2 trial was done at Sunnybrook Health Sciences Centre, Toronto, ON, Canada, and included patients with pathologically confirmed glioblastoma and planned for concurrent daily chemoradiotherapy up to 60 Gy in 30 daily fractions over 6 weeks (long course) or 40 Gy in 15 daily fractions over 3 weeks (short course). Eligible patients were adults (≥18 years) with an expected life expectancy greater than 12 weeks and an Eastern Cooperative Oncology performance status less than or equal to 2. A 5 mm clinical target volume (CTV) was applied, with the allowance of associated T2-weighted fluid-attenuated inversion recovery hyperintense regions in a personalised way at the discretion of the treating physician. All patients were treated with 1·5 T MRI-guided linear accelerator (MR-Linac) incorporating weekly gadolinium-enhanced online adaptive fractions. The primary outcome was the risk of marginal failure powered for non-inferiority with a margin of 10% compared with a historical control. All patients were included in the primary and safety analyses. This study is registered with ClinicalTrials.gov, NCT04726397.

Findings: Between April 28, 2021, and May 12, 2023, 109 patients were assessed for eligibility and 98 were enrolled and received treatment on the UNITED protocol with 59 [60%] patients receiving long-course radiotherapy and 39 [40%] receiving short-course radiotherapy. Median follow-up was 14·2 months (IQR 8·9–19·7). 53 (54%) of 98 patients were male and 45 (46%) were female. The observed risk of marginal failure was 4% (95% CI 0–8). The most common grade 3–4 adverse events were lymphopenia (eight [11%] of 72 patients without baseline lymphopenia) and thrombocytopenia (four [4%] of 98 patients). Serious adverse events occurred in one (1%) patient due to febrile neutropenia and there were no treatment-related deaths.

Interpretation: MRI-guided adaptation for glioblastoma enables margin de-escalation and resulted in a low rate of marginal failure. A randomised trial comparing this technique to a standard large-margin radiotherapy approach will establish whether toxicity and quality-of-life improvements can be realised.

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**.

Qiu Y, Li Y, Jiang C, Wu X, Liu W, Fan C, Ye X, He L, Xiao S, Zhao Q, Wu W, Chen K, Tan C, Li Y, Wang H, Liu F.

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.

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.

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cIMPACT-NOW Update 12: Refining pathology-based risk stratification and grading for IDH-mutant gliomas.

Brat DJ, Aldape K, French PJ, Louis DN, Nasrallah MP, Reifenberger G, Reuss DE, Touat M, van den Bent MJ, Wesseling P, Figarella-Branger D.

Neuro Oncol. 2026 Sep 1;28(9):2069-2089. doi: 10.1093/neuonc/noag108.

A working group of cIMPACT-NOW evaluated the literature on IDH-mutant gliomas for opportunities to improve pathology-based risk stratification and grading, especially at the interface of CNS WHO grades 2 and 3, since therapeutic decisions depend on risk assessment for clinical management. The group also evaluated newly described IDH-mutant glioma subgroups and considered multidisciplinary aspects of therapeutic decision-making. PDGFRA amplification was associated with highly aggressive clinical behavior of IDH-mutant astrocytomas, consistent with CNS WHO grade 4. Other genetic alterations associated with intermediate risk and most consistent with CNS WHO grade 3 included PIK3 mutations; EGFR alteration; MYCN amplification; and specific retinoblastoma pathway alterations, including CDK4, CDK6, and CCND2 amplification, RB1 homozygous deletion or mutation, and mutation of CDKN2A. DNA methylation signatures of G-CIMP-low or A_IDH_HG were consistent with CNS WHO grade 3 or 4, depending upon other grading criteria. We suggest a mitotic count of ≥3 per 2.4 mm2 could be considered as a CNS WHO grade 3 criterion. Our review did not uncover features to improve the grading of oligodendroglioma, IDH-mutant and 1p/19q-codeleted, although CNS WHO grade 3 tumors with elevated mitotic rates, yet lacking necrosis, microvascular proliferation, CDKN2A/B homozygous deletion, and MRI contrast enhancement, may be associated with extended survival. Implementing evidence-based criteria for risk stratification and grading will improve guidance for clinical decision-making.

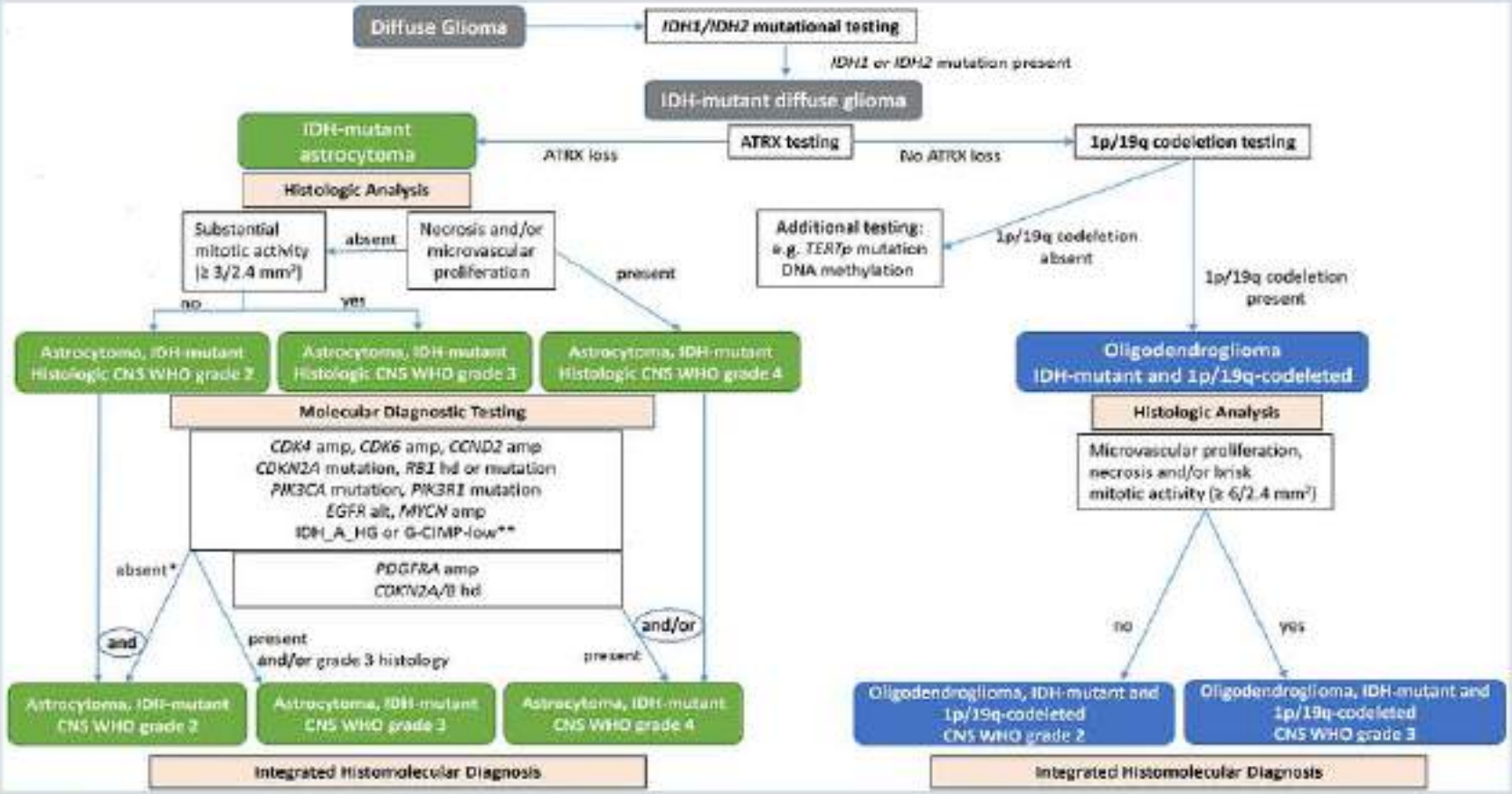


Figure 1. Schematic diagram demonstrating proposed decision tree for classification and grading of IDH-mutant gliomas. Molecular testing for grading should be undertaken in the context of the overall features of the case, together with the practice patterns and resource availability of the institution. The integrated histomorphologic diagnosis of astrocytoma, IDH-mutant, CNS WHO grade 2 is established by the presence of histologic grade 2 features and the absence of higher-grade histologic and molecular features (see text, Grading considerations). However, extensive molecular diagnostic testing may not be necessary in every case if the biologic potential is expected to be very low based on clinical, neuroimaging and histopathologic features. Molecular testing may be informative in these cases and should be pursued when there are ambiguous/borderline histological features between CNS WHO grade 2 and 3, contrast-enhancement or relatively rapid progression based on neuro-imaging, or unusual clinical characteristics. For the integrated histomorphologic diagnosis of astrocytoma, IDH-mutant, CNS WHO grade 3, the presence of grade 3 histology and/or the presence of molecular features consistent with grade 3 are sufficient. For the integrated histomorphologic diagnosis of astrocytoma, IDH-mutant, CNS WHO grade 4, the presence of grade 4 histology and/or the presence of molecular features consistent with grade 4 are sufficient. Abbreviations: amp, amplification; alt, alteration (amplification or mutation); hd, homozygous deletion; *TERTp*, *TERT* promoter. *as indicated (see text); ** the finding of G-CIMP-high or A_IDH does not always indicate grade 2 clinical behavior.

Table 2. Molecular alterations suggesting higher-grade (CNS WHO grade 3 or 4) IDH-mutant astrocytoma

CDK4 amplification
CDK6 amplification
CCND2 amplification
RB1 homozygous deletion or mutation
CDKN2A mutation
PIK3CA or *PIK3R1* mutation
EGFR alteration (amplification or mutation)
MYCN amplification
DNA methylation signature of G-CIMP-low or A_IDH_HG
PDGFRA amplification[a]
CDKN2A/B homozygous deletion[a]

[a]CNS WHO grade 4.

Early palliative care for patients with glioblastoma: A randomized phase III **clinical trial** (EPCOG).

Golla H, Nettekoven C, Hellmich M, Appelmann I, Bausewein C, Becker G, Boehlke C, Brumbarova T, Civello D, Clusmann H, Haberland B, Heiland DH, Herrlinger U, Jaspers B, Joshi M, Mülller D, Müller W, Na CH, Neukirchen M, Radbruch L, Rapp M, Rolke R, Ruge M, Sabel M, Schnell O, Schwartz J, Thon N, Vatter H, von Baumgarten L, Voltz R, Goldbrunner R; EPCOG Study Group.

Neuro Oncol. 2026 Jan 1;28(1):226-240. doi: 10.1093/neuonc/noaf230.

Abstract

Background. Positive effects of early integration of palliative care (EIPC) have been shown for systemic solid malignant tumors. We tested the hypothesis that EIPC improves quality of life (QoL), palliative care (PC) problems and mood in glioblastoma patients and reduces caregiver burden.

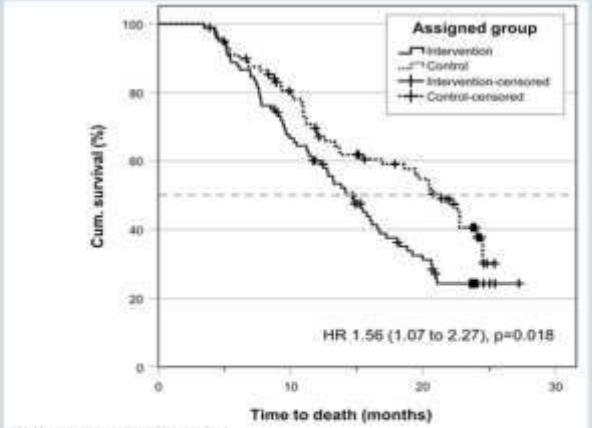
Methods. This randomized, rater-blinded, controlled trial conducted in six German university medical centers included glioblastoma patients within four weeks after diagnosis (first/recurrent) and their caregivers. Patients received standard care (control) or standard care and EIPC (intervention) for 12 months. Primary outcome was change in QoL after six months measured by the trial outcome index of the FACT-Br. Data were assessed 3-monthly for up to 24 months.

Results. Between 05/2019 and 04/2021 patients were enrolled and randomized to the intervention (n=109) or control group (n=108). QoL at month six was in favor of the intervention, however not statistically significant (mean difference 4.1 with 95% CI, −4.4 to 12.6, P=.34; intervention: n=98 (m=54/f=44); control: n=89 (m=50/f=39)). In an analysis adjusted for time of death, performed because of a significant survival difference (control superior to intervention, P=.018), QoL was better in the intervention group (P=.041). Secondary outcomes showed that patients significantly benefited from EIPC regarding PC problems and mood especially after intervention ended, while caregivers did not seem to benefit.

Conclusions. Provided that the survival difference is included in the analysis, EIPC improves QoL in glioblastoma patients. This, in addition to improved mood and PC problems, demonstrates that EIPC sustainably improves 'how to live' but not 'length of life'.

Key Points

- First randomized controlled trial on early palliative care in glioblastoma patients
- Shorter overall survival in the intervention group
- Positive effects on psychosocial, mood, palliative care, and quality of life aspects



Numbers at risk (censored)

Intervention	98 (0)	91 (2)	62 (2)	40 (5)	24 (3)	3 (16)	0 (3)
Control	89 (0)	83 (1)	66 (6)	47 (5)	38 (4)	1 (27)	0 (1)

Figure 2. Kaplan-Meier estimates of cumulative overall survival according to treatment group (modified intention-to-treat (mITT) population). Solid line = intervention group, dotted line = control group; HR = hazard ratio.

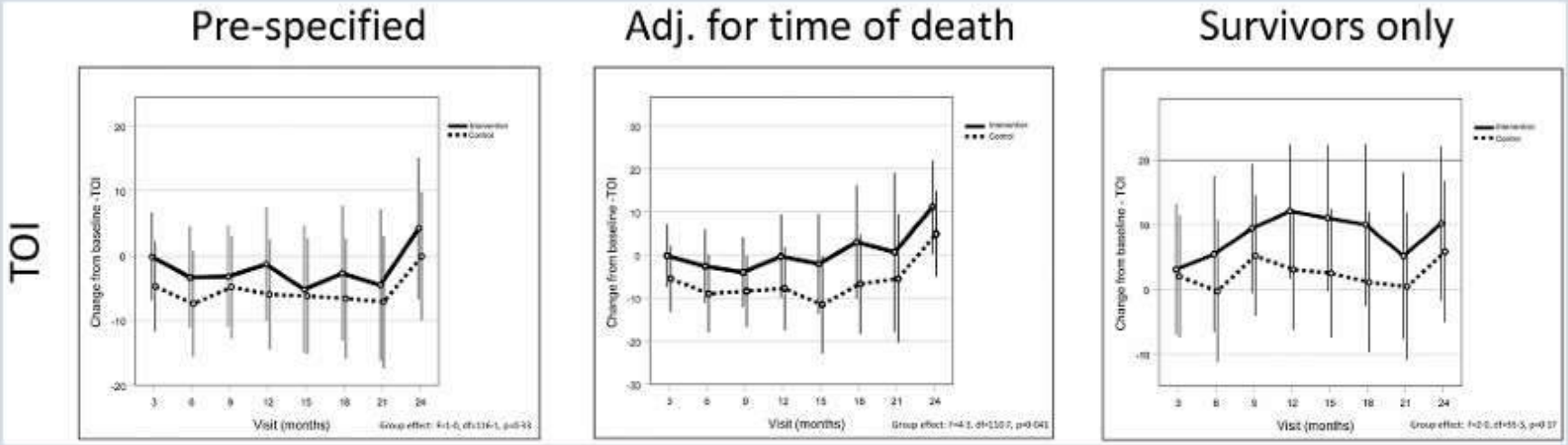


Figure 3. Change in the Trial Outcome Index (TOI) of the Functional Assessment of Cancer Therapy-Brain (FACT-Br) from baseline (EMM with 95% CI). Change = post value (month 3-24) minus baseline value. Higher scores indicating better QoL with respect to physical, functional and brain specific factors; range of TOI 0-148. Solid line: intervention, dotted line: control, EMM = estimated marginal mean, CI = confidence interval.

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Temozolomide Versus Radiotherapy as First-Line Therapy for **Low-Grade Glioma**: Mature Results of a Randomized Phase III **Trial** (EORTC 22033-26033/NCIC-CTG/TROG/MRC-CTU).

Baumert BG, Hegi ME, van den Bent MJ, von Deimling A, Gorlia T, Hoang-Xuan K, Brandes AA, Sargos P, Taphoorn MJB, Vauleon E, Phillips C, Kros JM, Bady P, Wick W, Enting R, Reni M, Thiessen B, Dhermain F, Bromberg JE, Jacob J, Reijneveld JC, Chinot O, Gijtenbeek JMM, Rossiter JP, Balana C, Azevedo ALS, Clement PM, Berghoff A, Tzuk-Shina T, Weller M, Nordal RA, Rees J, Lacombe DA, Mason WP, Stupp R.

J Clin Oncol. 2026 Jul 2:JCO2502735. doi: 10.1200/JCO-25-02735. Online ahead of print.

Purpose: Prognosis in low-grade gliomas (LGGs) remains highly variable, and treatment-related late toxicity is a concern. This trial was comparing single-modality therapies in patients who often survive for years or decades and investigating differential responses according to molecular markers.

Methods: Four hundred seventy-eight patients with clinical high-risk LGG (WHO grade 2) were randomly assigned to standard radiotherapy (RT; 28 × 1.8 Gy) or dose-dense temozolomide (TMZ; 75 mg/m^2 once daily × 21/28 days, up to 12 cycles).

Results: There was no significant difference in progression-free survival or overall survival (OS) between study arms. Analyzable tumor tissue in 73% (351/478) of patients allowed for post hoc reclassification according to the 2021 WHO pathologic criteria. In astrocytoma, IDHmt/1p/19q noncodeleted (n = 178), median OS was similar, 6.6-6.7 years irrespective of arm (0.67-1.44, *P* = .93). In oligodendroglioma, IDHmt/1p/19q codeleted (n = 109), median OS was 12.9 years (9.4-not reached) with RT and 14.9 years (10.1-number of events not reached) with TMZ (hazard ratio [HR], 0.88 [0.52-1.49], *P* = .63). In 64 tumors without isocitrate dehydrogenase (IDH) mutations, survival favored the TMZ arm: OS 2.5 (1.8-3.3) versus 4.7 (2.2-7.2) years (HR, 0.47 [0.27-0.82], *P* = .0068). Patients age 40 years and older fared better than patients younger than 40 years, challenging the current notion of age alone as a negative prognostic factor.

Conclusion: The assigned initial treatment modality did not affect progression-free survival or OS, regardless of the molecular subtype. Combined-modality therapy was not tested in this trial but has since become a standard of care for IDH-mutant astrocytoma. With emerging novel therapeutic options, rational treatment strategies tailored at the individual clinical and pathologic recurrence risk profiles will be needed. The validity of an age cutoff as prognostic factor is challenged when tumors are molecularly classified.

Health-related quality of life and cognitive functioning in survivors of oligodendroglioma: An international cross-sectional investigation.

Boele FW, Frances SM, Darlix A, Ducray F, Cartalat S, Guerdoux E, Tabouret E, Burger MC, Rydén I, Malmstrom A, Vauleon E, Kazda T, Renovanz M, Werner JM, Welsh L, Sanghera P, Dehais C, Desideri I, McBain C, Mehta S, Lord H, Jena R, Foweraker K, Ashkan K, Engelhardt J, Bourg V, Herrlinger U, Lawson McLean A, Hertler C, Haldbo-Classen L, Dahlrot RH, Noel G, Durando X, Hrab I, Razis E, Weller M, Muhic A, Klein M.

Neuro Oncol. 2025 Nov 1;27(11):2959-2974. doi: 10.1093/neuonc/noaf172.

Background: Patients with oligodendroglioma have a relatively favorable prognosis. The long-term impacts of the tumor itself and its treatment on health-related quality of life (HRQOL) and cognition remain largely unclear. We investigated associations between treatment and functioning of survivors of oligodendroglioma.

Methods: In this cross-sectional observational study, patients with oligodendroglioma, isocitrate dehydrogenase-mutant and 1p/19q-codeleted, diagnosed ≥ 5 years ago, were recruited. Patients completed patient-reported outcome measures (EORTC QLQ-C30; BN20; MOS Cognitive Complaints Scale) and cognitive tests (HVLT-R, TMT, COWAT). Associations between HRQOL and cognition outcomes, and clinical variables (time since diagnosis; age at diagnosis; progression; tumor location; treatments delivered; time since treatment; current medication) were explored with regression analyses.

Results: In total, 237 patients M = 9.9 years postdiagnosis (SD = 4.2, range 5.0-25.8) took part from 33 sites across 9 countries. Clinically relevant levels of impairment were noted in >40% of patients on EORTC QLQ-C30 scales for cognitive functioning (56.1%), emotional functioning (49.8%), fatigue (45.1%), and physical functioning (40.5%). In individuals, cognitive impairment ranged from 17.7% for processing speed to 46.0% for episodic verbal memory (delayed recall). Among other clinical factors such as current use of antiseizure medication or antidepressants, age, disease progression, time since diagnosis and time since treatment, and radiotherapy treatment (ever received) was linked to HRQOL and cognitive functioning outcomes (posthoc analyses for cumulative radiotherapy dose: not significant).

Conclusions: In oligodendroglioma survivors, HRQOL and cognitive impairment are prevalent even years into follow-up. Supportive care and rehabilitation should be prioritized to mitigate these challenges and improve daily functioning.

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.

Fangusaro J, Onar-Thomas A, Young Poussaint T, Lensing S, Ligon AH, Lindeman N, Banerjee A, Kilburn LB, Lenzen A, Pillay-Smiley N, Pollack IF, Robison NJ, Partap S, Qaddoumi I, Landi D, Jones DTW, Stewart CF, Fouladi M, Dunkel IJ.

Neuro Oncol. 2025 Oct 14;27(9):2415-2428. doi: 10.1093/neuonc/noaf065.

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); the 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.

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Phase I/II and window-of-opportunity study of pamiparib and metronomic temozolomide for recurrent isocitrate dehydrogenase mutant **gliomas**.

Schiff D, Ye X, Li J, Ellingson BM, Wen PY, Walbert T, Campian J, Nabors LB, Ozer BH, Desai A, Omuro A, Desideri S, Danda N, Grossman S, Bindra RS.

Neuro Oncol. 2026 Feb 1;28(2):485-494. doi: 10.1093/neuonc/noaf246.

Background: Preclinical studies demonstrate activity of poly(adenosine 5'-diphosphate-ribose) polymerase (PARP) inhibitors in isocitrate dehydrogenase (IDH) mutant gliomas. We investigated safety, tolerability, pharmacokinetics, and efficacy of the PARP inhibitor pamiparib in conjunction with metronomic low-dose temozolomide in patients with recurrent IDH mutant (IDHmt) gliomas in a multicenter Phase I/II/window of opportunity study.

Methods: Patients received pamiparib in conjunction with daily temozolomide. Following Phase I determination of maximum tolerated dose (MTD), we enrolled 2 patient cohorts (Arm A, multiple prior chemotherapy regimens; Arm B, single prior regimen) in a 2-stage design. Exploratory cohorts examined grade 4 IDHmt patients and intratumoral pharmacokinetics of pamiparib. The primary endpoint was objective radiographic response (ORR) by RANO criteria.

Results: Sixty-six subjects were enrolled. We established pamiparib 60 mg twice daily with temozolomide 20 mg daily as the phase II dose. In non-enhancing and enhancing tumor, pamiparib exhibited an unbound tumor/plasma ratio of 0.92 and 0.98, respectively. 0/15 Arm A and 1/24 Arm B patients achieved a centrally confirmed partial response. Median progression-free survival for Arm A was 5.9 months (95% CI, 1.2-14.8 months), and for Arm B was 9.7 months (95% CI, 5.7-21.7 months). Grade 3+ anemia and neutropenia affected 24% and 33% of patients, respectively. Twenty-two of 66 patients (33.3%) discontinued study treatment for reasons other than tumor progression.

Conclusions: Pamiparib appeared to achieve sufficient pharmacologically active concentrations in both enhancing and non-enhancing tumors. While some patients achieved prolonged progression-free survival, combination with temozolomide did not produce a meaningful ORR in IDHmt recurrent gliomas. Cumulative hematologic toxicity was substantial and impacted long-term tolerability.

Erdafitinib in Patients With Advanced Solid Tumors With *FGFR* Alterations (RAGNAR): Results of Tumor-Specific Analyses and Secondary Cohorts.

Carranza O, Pant S, Schuler M, Witt O, Geoerger B, Loriot Y, Farouk Sait S, Arnold D, Dal Molin GZ, Lugowska I, Winter H, Baldini C, Corassa M, Thomas S, Crow L, Xia Y, Triantos S, Sweiti H, Reardon DA.

JCO Precis Oncol. 2026 Jul;10(7):e2501094. doi: 10.1200/PO-25-01094. Epub 2026 Jul 15.

Purpose: Erdafitinib, a pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor, is approved for second-line treatment of locally advanced or metastatic urothelial carcinoma with susceptible *FGFR3* alterations. Primary histology-agnostic analysis from the phase II RAGNAR study (ClinicalTrials.gov identifier: NCT04083976) indicated a clinical benefit with erdafitinib in Broad Panel Cohort (BPC) patients. We present tumor-specific updated efficacy and safety results from the BPC and tumor-agnostic findings from the Exploratory and Pediatric Cohorts of RAGNAR.

Methods: The Broad Panel, Exploratory, and Pediatric Cohorts enrolled patients with target (selected) *FGFR* alterations, nontarget *FGFR* alterations, and any *FGFR* alterations, respectively. Adults and pediatric patients (6 years and older) with advanced, unresectable, or metastatic disease who progressed after ≥1 prior line of systemic therapy and exhausted standard therapies were eligible. Erdafitinib 3-8 mg once daily (with possible uptitration) was administered orally until disease progression or intolerable toxicity.

Results: Objective response rates (ORRs) in the BPC were 10.0% (3 of 30) for high-grade glioma, 26.1% (6 of 23) for non-small cell lung cancer, 28.6% for (2 of 7) low-grade glioma, 31.3% (5 of 16) for breast cancer, 33.3% (5 of 15) for head and neck squamous cell carcinoma, 55.6% (10 of 18) for pancreatic cancer, and 100% (5 of 5) for salivary gland cancer. The ORR was 3.8% (2 of 53) in the Exploratory Cohort. In the Pediatric Cohort (n = 11), there were one responder and seven patients with durable stable disease. Treatment-related adverse events (TRAEs) were consistent with the known safety profile of erdafitinib. Pediatric-specific TRAEs included epiphysiolysis and limb fracture.

Conclusion: Encouraging activity was observed for erdafitinib across tumor types in patients with advanced malignancies and selected *FGFR* alterations who have exhausted treatment options. More limited activity was observed for erdafitnib in the Exploratory Cohort.

Clinical outcomes of adding vincristine to procarbazine-lomustine in patients with gliomas: insights from current evidence.

Pinzón-Ramírez V, Cueva-Cañola LE, Natera DE, Olivera HEA, Camacho-Hernández OE, Beltran-De la Fuente AC, Ramirez-Alvarez SA, Cubas EYG, Flores GV, Gamez ME, Castilla LR.

Ecancermedicalscience. 2026 May 1;20:2115. doi: 10.3332/ecancer.2026.2115. eCollection 2026.

Background: Temozolomide (TMZ) is the standard chemotherapy for gliomas due to good tolerability. Clinical studies suggest a combination of procarbazine, lomustine (CCNU) and vincristine (PCV) provides superior survival and progression delay, but toxicities limit use. Given the ongoing debate over the role of vincristine in glioma chemotherapy amid the dominance of TMZ, simplified procarbazine and CCNU (PC) regimens warrant renewed evaluation.

Methods: Three databases were searched up to August 2025 to identify studies that directly compared PC and PCV in patients with low-grade and high-grade gliomas. Outcomes included progression-free survival (PFS), overall survival (OS) and treatment-related toxicities. Hazard ratios (HRS) and relative risks (RRS) were then pooled using a random-effects model.

Results: In a total population of 301 patients with low- and high-grade gliomas, PC significantly reduced the risk of disease progression compared with PCV (HR = 0.72, 95% confidence interval (CI): 0.53-0.98; $p = 0.04$) and OS was also significantly longer with PC (HR = 0.59, 95% CI: 0.37-0.95; $p = 0.03$). Neurotoxicity (RR = 0.12, 95% CI: 0.02-0.63; $p = 0.01$) and treatment discontinuation (RR = 0.11, 95% CI: 0.02-0.80; $p = 0.03$) were less frequent with PC.

Conclusion: With the limited evidence available to date, we found that PC achieved significantly longer PFS and OS than PCV, while maintaining a better safety profile. We recommend further well-designed and adequately powered randomised clinical trials directly comparing TMZ, PC and PCV to determine which patient populations and glioma subtypes - according to the current World Health Organisation 2021 classification - derive the greatest survival benefit and tolerability from each regimen.

Key points: Procarbazine-lomustine combination (PC) shows superior progression-free survival and overall survival versus procarbazine, lomustine and vincristine (PCV) in gliomas.Omitting vincristine may improve efficacy and reduce neurotoxicity.Findings suggest PC could be a safer alternative, pending confirmation by randomised controlled trials.

Importance of the study: This meta-analysis is the first to directly evaluate whether vincristine is necessary within the procarbazine, lomustine and vincristine (PCV) regimen for gliomas. By synthesising data from three retrospective cohorts, it demonstrates that the procarbazine-lomustine combination (PC) achieved significantly longer progression-free and overall survival compared with PCV, while markedly reducing neurotoxicity and treatment discontinuation. These findings challenge the traditional view that vincristine is an indispensable component of chemotherapy for diffuse gliomas. Given that temozolomide has become the preferred agent in contemporary practice, clarifying the relative contributions of PC, PCV and TMZ remains essential for optimising therapeutic strategies. Although limited by the small number and retrospective design of included studies, this analysis suggests that PC may represent a more effective and tolerable alternative, underscoring the need for prospective randomised trials in the modern molecular era of glioma classification.

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Seizure prophylaxis in **glioma** surgery (SPRING): A multi-center, unblinded, randomized **trial**.

Jenkinson MD, Bulbeck H, Burns J, Rooney AG, Dobbie R, Carruthers J, Lessels S, Watson R, Gribben C, Robinson T, Vale L, Thompson G, Erridge SC, Watts C, Marson AG, Grant R; SPRING study Collaborators.

Neurooncol Pract. 2025 Nov 5;13(2):252-261. doi: 10.1093/nop/npaf114. eCollection 2026 Apr.

Background: 50%-80% of glioma patients will have seizures. Guidelines recommend against prophylactic anti-seizure medication, but levetiracetam is frequently prescribed. Our aim was to determine the effectiveness of 12-month prophylactic levetiracetam at reducing seizure risk.

Methods: Seizure-naïve patients undergoing glioma surgery were randomized (1:1) to 12-month levetiracetam or no prophylaxis and followed until death or a maximum of 18-months. The primary outcome was 1-year risk of first seizure. Patients who died within 12 months of randomization without experiencing a seizure were excluded from the primary outcome analysis. Target accrual was 804 participants. The trial was registered (ISRCTN 49474281 and EudraCT 2018-001312-30).

Results: Between October 10, 2019 and August 30, 2022, 96 patients, from 24 to 79 years of age, were randomized to levetiracetam (n = 49) or no prophylaxis (n = 47). The trial closed early due to slow accrual and the Covid pandemic. In the levetiracetam group, 17 patients had a seizure and 32 did not (19 survived ≥12 months, 13 died within 12 months). In the no-prophylaxis group, 15 patients had a seizure and 30 did not (21 survived ≥12 months, 9 died within 12 months). Seventeen of the 36 evaluable levetiracetam patients (47%) had a seizure, compared with 15 of 36 evaluable no-prophylaxis patients (41%) (OR: 1.25, 95% CI, 0.49-3.21, P = .64). There were no levetiracetam-related serious adverse events.

Conclusions: The seizure prophylaxis in glioma surgery (SPRING) trial provides no evidence of a difference between levetiracetam and no prophylaxis in the 12-month seizure risk in patients undergoing glioma surgery, but the study was underpowered. The role of prophylactic anti-seizure medication remains undefined.

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

Baumert BG, P M Jaspers J, Keil VC, Galldiks N, Izycka-Swieszewska E, Timmermann B, Grosu AL, Minniti G, Ricardi U, Dhermain F, Weber DC, van den Bent M, Rudà R, Niyazi M, Erridge S.

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

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.

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cIMPACT-NOW Update 12: Refining pathology-based risk stratification and **grading** for IDH-mutant **gliomas**.

Brat DJ, Aldape K, French PJ, Louis DN, Nasrallah MP, Reifenberger G, Reuss DE, Touat M, van den Bent MJ, Wesseling P, Figarella-Branger D.

Neuro Oncol. 2026 Sep 1;28(9):2069-2089. doi: 10.1093/neuonc/noag108.

A working group of cIMPACT-NOW evaluated the literature on IDH-mutant gliomas for opportunities to improve pathology-based risk stratification and grading, especially at the interface of CNS WHO grades 2 and 3, since therapeutic decisions depend on risk assessment for clinical management. The group also evaluated newly described IDH-mutant glioma subgroups and considered multidisciplinary aspects of therapeutic decision-making. PDGFRA amplification was associated with highly aggressive clinical behavior of IDH-mutant astrocytomas, consistent with CNS WHO grade 4. Other genetic alterations associated with intermediate risk and most consistent with CNS WHO grade 3 included PIK3 mutations; EGFR alteration; MYCN amplification; and specific retinoblastoma pathway alterations, including CDK4, CDK6, and CCND2 amplification, RB1 homozygous deletion or mutation, and mutation of CDKN2A. DNA methylation signatures of G-CIMP-low or A_IDH_HG were consistent with CNS WHO grade 3 or 4, depending upon other grading criteria. We suggest a mitotic count of ≥3 per 2.4 mm2 could be considered as a CNS WHO grade 3 criterion. Our review did not uncover features to improve the grading of oligodendroglioma, IDH-mutant and 1p/19q-codeleted, although CNS WHO grade 3 tumors with elevated mitotic rates, yet lacking necrosis, microvascular proliferation, CDKN2A/B homozygous deletion, and MRI contrast enhancement, may be associated with extended survival. Implementing evidence-based criteria for risk stratification and grading will improve guidance for clinical decision-making.

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Targeted therapies plus radiotherapy for diffuse intrinsic pontine **glioma**: the randomized phase 2 BIOMEDE **trial**.

Debily MA, Le Teuff G, Kergrohen T, Varlet P, Castel D, Leblond P, Hargrave D, Nysom K, Blomgren K, McCowage GB, Bautista F, van Vuurden D, Jones C, Mackay A, Izquierdo E, Ziegler DS, Moussa A, Barret E, Puget S, Beccaria K, Aquilina K, Riffaud L, Bolle S, Abbou S, Bertozzi AI, De Carli E, Boddaert N, Dangouloff-Ros V, Calmon R, Blanc P, Vassal G, Le Deley MC, Grill J.

Nat Med. 2026 Jun;32(6):2201-2215. doi: 10.1038/s41591-026-04354-1. Epub 2026 Apr 24.

Diffuse intrinsic pontine glioma (DIPG) is the pediatric tumor with the worst prognosis. BIOMEDE was a randomized phase 2 trial comparing the efficacy in terms of overall survival (OS) (primary endpoint) of epidermal growth factor receptor (EGFR) inhibitor erlotinib, mTOR inhibitor everolimus and multitargeted tyrosine kinase inhibitor dasatinib in combination with radiotherapy in patients with a biopsy-proven DIPG. Tumors were assessed centrally for immunohistochemical biomarkers (EGFR overexpression or PTEN loss) together with whole-exome and RNA sequencing. A cohort of 66 children with the same inclusion criteria and treated previously with temozolomide-based regimen was used to compare outcome. Treatment allocation was performed by randomization in 233 patients, designed so that a drug could not be allocated if the corresponding biomarker was absent: 36 received erlotinib, 102 received dasatinib and 95 received everolimus. The trial was ended for futility of the primary endpoint following the recommendations of the independent data monitoring committee: OS from biopsy was not different from the control cohort (median OS = 10.8 months (95% confidence interval (CI): 9.5-13.0)) in any of the three arms (median OS = 9.7 months (95% CI: 7.8-14.6) for erlotinib; 9.9 months (95% CI: 8.8-11.2) for dasatinib; and 11.9 months (95% CI: 10.7-14.2) for everolimus). Everolimus showed significantly less ocular, renal, skin and gastrointestinal side effects and treatment discontinuation for toxicity (secondary endpoint). TP53 mutations, frequently linked to multiple structural chromosomal aberrations, were the strongest predictor for poor survival in multivariate analysis (hazard ratio = 2.8 (95% CI: 1.9-4.2), P < 0.0001). Both mutations in and activation of the mTOR pathway were associated with a better response to everolimus. Four long-term survivors treated with an mTOR inhibitor were alive free of treatment over 6 years from diagnosis. With comprehensive tumor profiling, BIOMEDE validated prognostic biomarkers as well as informative theranostic biomarkers for future trials. ClinicalTrials.gov: NCT02233049 .

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Diagnostic yield, safety, and molecular-era clinical utility of stereotactic biopsy for **brainstem** lesions: a contemporary systematic **review** and meta-analysis.

Du H, Wang J, Liu Q, Luo G.

Front Surg. 2026 Sep 9;13:1953479. doi: 10.3389/fsurg.2026.1953479. eCollection 2026.

Background/objectives: Stereotactic biopsy of brainstem lesions must balance diagnostic and molecular information against procedure-related neurological risk. We updated the evidence base after a reviewer-directed literature coverage and overlap audit.

Methods: This PRISMA 2020 systematic review and meta-analysis was registered in PROSPERO (CRD420261432357). Searches covered English and Chinese bibliographic databases, trial registries, and Google Scholar, with forward and backward citation tracking during revision. Diagnostic yield ar overall complications were analyzed with logit random-effects models; permanent neurological morbidity and procedure-related mortality were analyzed with binomial-normal generalized linear mixed models (GLMMs). Molecular clinical utility was synthesized narratively because its constructs and denominators were heterogeneous.

Results: Seventy-six reports met review-level eligibility (71 full-text and 5 abstract/conference reports), and 55 independent studies contributed to at least one preferred quantitative synthesis. Diagnostic yield was 1,814/1,956, with a pooled estimate of 93.5% (95% CI, 91.5%-95.0%). Overall complications were 162/1,797, with a pooled estimate of 10.5% (95% CI, 8.5%-12.8%). Permanent neurological morbidity was reported in 17 compatible studies (14/859; GLMM 0.83%, 95% CI, 0.22%-3.03%). Procedure-related mortality was 11/1,765 (crude 0.62%, exact 95% CI, 0.31%-1.11%); the primary GLMM estimate was 0.30% (95% CI, 0.07%-1.24%), whereas continuity-corrected model produced higher estimates. Diagnostic yield remained 93.7% (95% CI, 91.3%-95.5%) after excluding studies with fewer than 20 participants, although observed yield was inversely associated with study size.

Conclusions: In selected published cohorts, stereotactic biopsy provided high diagnostic yield. Overall complications were clinically meaningful, while observed procedure-related mortality was below 1% and permanent morbidity was uncommon but imprecisely estimated. Population, era, technique, outcome definition, and small-study analyses support cautious individualized interpretation rather than a universal biopsy recommendation.

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First report of a **clinical** and radiologic response to vorasidenib in a patient with isocitrate dehydrogenase-mutant **brainstem** astrocytoma.

Kim H, Gomez A, Dixit KS.

Neurooncol Pract. 2025 Dec 31;13(2):428-431. doi: 10.1093/nop/npaf131. eCollection 2026 Apr.

Background: IDH (isocitrate dehydrogenase)-mutant gliomas of the brainstem are exceedingly rare. In the INDIGO trial, patients with brainstem gliomas were excluded, thus, no data exists on the use of vorasidenib in this group.

Case summary: We describe the case of a 20-year-old female who developed progressive left facial myokymia and binocular horizontal diplopia on leftward gaze over two years. Brain MRI demonstrated a non-enhancing, expansile T2/FLAIR hyperintense lesion in the left greater than right brainstem extending from the dorsal pons into the cervicomedullary junction. The slowly progressive nature of her symptoms and radiologic appearance were most suggestive of a lower-grade, infiltrative neoplasm. She underwent biopsy of the left middle cerebellar peduncle, which confirmed an IDH R132C-mutant astrocytoma, WHO grade 2. With shared decision making, the patient elected to initiate therapy with vorasidenib 40 mg once daily. After six months of treatment, her diplopia and facial myokymia nearly resolved. By eleven months, her symptoms remain well controlled. Brain MRI shows significant reduction in the size of the T2/FLAIR hyperintense lesion.

Conclusions: This case is the first to report a favorable clinical and radiologic response to vorasidenib in a patient with an IDH-mutant brainstem astrocytoma, suggesting the potential use of IDH inhibitors in this group.

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Astroblastoma

A Case of Spinal **Astroblastoma**-Like Neuroepithelial Tumor With MAMLD1::BEND2 Fusion.

Inoue Y, Nakashima T, Shirakura T, Otani Y, Sasada S, Ishida J, Tanaka T, Miyahira A, Hibiya Y, Yoshioka T, Hirato J, Ichimura K, Suzuki H, Nobusawa S, Tanaka S.

Pathol Int. 2026 Jan;76(1):e70075. doi: 10.1111/pin.70075. Epub 2025 Dec 29.

Frontoparietal **astroblastoma** with MN:1BEND2 fusion in a young woman: A case report.

Saroya AA, Ejaz ZH, Attique U, Memon AH, Anwar SSM, Khan AA.

Surg Neurol Int. 2026 Apr 17;17:227. doi: 10.25259/SNI_85_2026. eCollection 2026.

Astroblastoma-like tumor with an EWSR1::BEND2 fusion in the fourth ventricle: a case report and narrative review.

Yao X, Yang L, Shen M, Wei Y, Chen N, Zhang Z.

Childs Nerv Syst. 2026 Jul 3;42(1):283. doi: 10.1007/s00381-026-07386-7.

Diagnostic pitfall: BCOR immunoreactivity in a molecularly confirmed **astroblastoma**, MN1-altered (HGNET-MN1).

Nisarga P, Rathore B, Hodjat P, Derinkuyu BE, Graham RT, Skoch J, Leino D, Gupta K.

Clin Neuropathol. 2026 Jan-Feb;45(1):32-35. doi: 10.5414/NP301715.

MN1 rearrangement detected by FISH analysis in a neuroepithelial tumor with EWSR1::PATZ1 demonstrating ependymoma-like and **astroblastoma**-like histology: A diagnostic pitfall.

Shirakura T, Yonezawa H, Arai Y, Hama N, Fukuoka K, Yamazaki A, Kirishima M, Yoshida A, Yokoo H, Shibata T, Hanaya R, Nobusawa S.

J Neuropathol Exp Neurol. 2026 Aug 4:nlag087. doi: 10.1093/jnen/nlag087. Online ahead of print.

Xanthoactrocytoma

Leptomeningeal Dissemination in TERT Promoter-mutant Anaplastic Pleomorphic **Xanthoastrocytoma** Responding to BRAF-MEK Inhibition: A Case Report.

Kitano R, Nagashima H, Goto H, Yamanishi S, Nishihara M, Tanaka K, Muragaki Y, Sasayama T.

NMC Case Rep J. 2026 Aug 14;13:393-399. doi: 10.2176/jns-nmc.2026-0094. eCollection 2026.

Identification of BRAF V600E Mutation in Cerebrospinal Fluid Aids in Diagnosing Leptomeningeal Carcinomatosis Arising From Pleomorphic **Xanthoastrocytoma**: A Case Report.

D'Amico RS, Avancena P, Kashanian A, Galvez R, Gruber D, Saba S, Zlochower A, Harshan M, Vojnic M.

Cancer Rep (Hoboken). 2026 Mar;9(3):e70487. doi: 10.1002/cnr2.70487.

Posttherapy [18F]FDOPA PET Findings in an Anaplastic Pleomorphic **Xanthoastrocytoma** With a BRAF V600E Mutation.

Passoni J, Rossi A, Milanaccio C, Piccardo A, Fiz F.

Clin Nucl Med. 2026 Sep 4. doi: 10.1097/RLU.0000000000006698. Online ahead of print.

CDKN2A/B status can be assessed by p16/MTAP immunohistochemistry as a practical surrogate in pleomorphic **xanthoastrocytoma** and high-grade astrocytoma with piloid features.

Simboli GA, Rousseau A, Basset L, Saffroy R, Hasty L, Sassi F, Métais A, Varlet P, Tauziède-Espariat A; RENOCLIP-LOC.

J Neuropathol Exp Neurol. 2026 Sep 23:nlag086. doi: 10.1093/jnen/nlag086. Online ahead of print.

PMID: 42777114

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Centre Eugène Marquis RENNES

Phase 3 randomized trial of postirradiation chemotherapy in patients with newly diagnosed **ependymoma**: A report from the Children's Oncology Group.

Smith AA, Onar-Thomas A, Lensing S, Dalton J, Bennett J, Tatevossian RG, Bertrand K, Lindsay H, Tabori U, Owens-Pickle E, Blackburn PR, Handler MH, Chambwe N, El Khoury L, Lau C, Kunin-Batson A, Sands S, Wu S, Zhou T, Chang A, Merchant TE, Leary S, Fouladi M, Gajjar A, Pollack IF, Foreman NK, Ellison DW.

Neuro Oncol. 2026 May 1;28(5):1286-1297. doi: 10.1093/neuonc/noaf285.

Background: The utility of chemotherapy for childhood ependymoma is uncertain without a prior randomized trial.

Methods: ACNS0831, a multicenter phase 3 randomized study conducted through the Children's Oncology Group (COG), included patients 1-21 years with newly diagnosed intracranial ependymoma. Patients with complete/near-total resections (GTR/NTR) or complete response (CR) to induction therapy were randomized to radiation (RT) alone or RT followed by chemotherapy (RT-CHEMO). Primary outcomes were event-free survival (EFS) and overall survival (OS). Due to anticipated noncompliance with chemotherapy, an "as treated" analysis was planned. Patients with subtotal resection (STR) were non-randomly assigned to RT-CHEMO. Grade 2 supratentorial tumors with GTR or CR to induction therapy were observed.

Results: Of 449 eligible patients, 325 with GTR/NTR or CR were randomized. Five-year EFS was 63.7% (95% CI: 55.1%-71.1%) for RT only (n = 161) versus 69.2% (60.8%-76.3%) for RT-CHEMO (n = 164) (1-sided log-rank P = .299, HR = 0.866). Five-year OS was 86.9% (79.8%-91.6%) for RT only versus 88.3% (81.8%-92.6%) for RT-CHEMO (1-sided log-rank P-value = .172, HR = 0.757). The "as treated" and "as randomized" analysis results were similar. Sixty-three subjects with STR were assigned to RT-CHEMO; 5-year EFS was 33.6% (22.1%-45.5%) and OS 74.0% (60.5%-83.5%). Supratentorial grade 2 tumors with GTR or CR were observed with a 5-year EFS of 66.9% (49.0%-79.7%) and OS of 100%. Molecular classification was provided for 94% (n = 422) of all subjects.

Conclusions: Primary analysis showed no benefit for maintenance chemotherapy. Further follow-up is important to assess its effect on late relapses. This is the largest cohort of molecularly classified ependymomas treated on a Phase 3 randomized trial.

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Clinical responses to trastuzumab deruxtecan in molecularly defined **ependymoma**.

Gonzalez Castro LN, Wu YC, Lin JR, Santiago-Ribeiro MJ, Laurenge A, Carpentier A, Coy S, Lin NU, Mokhtari K, Ligon KL, Touat M, Santagata S.

NPJ Precis Oncol. 2026 Jun 20. doi: 10.1038/s41698-026-01514-x. Online ahead of print.

Despite evidence that antibody drug conjugates (ADCs) are active in brain metastases, their role in primary central nervous system (CNS) tumors remains unclear. We report two adults with molecularly defined ependymoma - a MYCN-amplified spinal tumor with intracranial dissemination and a supratentorial ZFTA-RELA-fused tumor with multiple recurrences - who demonstrated radiographic response and/or durable clinical and metabolic stability with trastuzumab deruxtecan (T-DXd). HER2 expression was identified by immunohistochemistry in both tumors, consistent with prior systematic profiling of ADC targets in CNS tumors. Multiplexed imaging showed broad but heterogeneous HER2 expression across tumor states in both cases; in the MYCN-amplified tumor, this occurred alongside EGFR/MAPK-enriched proliferative niches, whereas the ZFTA-RELA tumor showed more diffuse organization without strong coupling of EGFR and proliferation. These findings provide early clinical evidence supporting HER2-directed ADCs in ependymoma and highlight the value of integrated molecular and spatial profiling in interpreting therapeutic response in rare CNS tumors.

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Molecular biology and phase 1 study of GM-CSF and intrathecal trastuzumab in children with recurrent -posterior fossa **ependymoma**.

Griesinger AM, Widener M, Donson AM, Mettetal A, Hankinson TC, Handler M, Mulcahy Levy JM, Lindsay HB, Macy ME, Foreman NK, Dorris K.

Neuro Oncol. 2026 Jul 1;28(7):1783-1793. doi: 10.1093/neuonc/noag066.

Background: Ependymoma (EPN) is an aggressive pediatric central nervous system tumor with poor survival and significant morbidity. As immune factors are associated with outcome, the potential for effective immunotherapy in posterior fossa (PF) EPN has been suggested. Based on the success of immune stimulants combined with an anti-GD2 monoclonal antibody in high-risk pediatric neuroblastoma, we hypothesized that a similar approach would be a plausible immunotherapy strategy for recurrent PF EPN.

Methods: A phase 0/1 trial evaluating the safety and dosing of intrathecal (IT) trastuzumab combined with subcutaneous (s.c.) granulocyte-macrophage colony-stimulating factor (GM-CSF) for pediatric patients with relapsed PF EPN was conducted.

Results: ErbB2/Her2, targeted by trastuzumab, was identified as a top therapeutic antibody target for EPN by in silico screening. In vitro co-culture assays with GM-CSF-stimulated autologous PBMCs showed trastuzumab antibody-dependent cell cytotoxicity in PFA EPN cell lines. A phase 1 clinical study identified that IT delivery of trastuzumab in combination with s.c. GM-CSF was safe in children at both dose levels tested. Four patients (57%) successfully completed all planned therapy. The median progression-free survival was 2.4 years (95% CI, 0.47, not evaluable). Profiling of biological correlates identified that tumors of patients who did not progress on the study had increased T-cell activity and decreased pro-tumor inflammatory myeloid gene expression compared to patients who progressed on study treatment.

Conclusion: IT trastuzumab in combination with GM-CSF is safe in recurrent pediatric PF EPN. A larger phase 2 study that includes both recurrent PFA and RELA-ST EPN is needed to determine the long-term efficacy of this immunotherapy strategy.

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Long-term outcomes and late effects of surgery and radiotherapy in adult intracranial **ependymoma** patients.

van de Langerijt ON, Ehret F, Niemierko A, Oh KS, Butler WE, Curry WT, Nahed BV, Haas-Kogan DA, Patel N, Marciscano AE, Rahman RM, Janssens GO, Shih HA.

J Neurooncol. 2026 Jun 25;178(3):78. doi: 10.1007/s11060-026-05680-7.

Purpose: To evaluate progression-free survival (PFS), overall survival (OS), local control (LC), and radiotherapy-related toxicities in the treatment of adult intracranial ependymoma.

Methods: A retrospective analysis was performed of WHO grade 2-3 adult intracranial ependymoma patients (≥ 18 years) treated with surgery alone or surgery and adjuvant radiotherapy between 2000 and 2024. Kaplan-Meier analyses were used to estimate PFS and OS. Acute and late treatment-related toxicities were characterized.

Results: Fifty-eight patients met the inclusion criteria. Median age was 39 years (interquartile range [IQR] 25-51), and median follow-up was 51 months (IQR 23-103). Overall, 76% were WHO grade 2, 74% had posterior fossa location, gross total resection was achieved in 60%, 88% received adjuvant local radiotherapy, and 5% received adjuvant chemotherapy. Five and 10-year PFS rates were 80% and 64%, respectively; 5 and 10-year OS rates were 92% and 85%, respectively. There were 13 (22%) recurrences: The location of first failure was local in nine, distant in two, and both local and distant in two. The 5-year LC rate was 82% (95% CI 67-90%), and the 10-year LC rate was 72% (95% CI 53-84%). The median time to local failure was 5.4 years. Ten (22%) patients experienced at least one grade ≥ 2 late treatment-related toxicity. One potential secondary glioma (grade 5) occurred after nine years.

Conclusion: In adult patients with intracranial ependymomas, surgery alone or surgery followed by radiotherapy resulted in relatively favorable long-term PFS, OS, and LC. Recurrences and late toxicities remain a concern.

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Effect of radiation on patients with grade 2 intramedullary spine **ependymoma**.

Ruchika F, Al-Mistarehi AH, Xia Y, Rajasekaran J, Albert AN, Ahmed AK, Jillala R, Raj D, Bettegowda C, Sciubba DM, L Lo SF, Bydon A, Witham T, Theodore N, Jallo G, Redmond KJ, Klienberg LR, Lubelski D.

Eur Spine J. 2026 Mar 7. doi: 10.1007/s00586-026-09756-w. Online ahead of print.

Purpose Spinal ependymomas are rare glial neoplasms. Given the rarity there is a lack of consensus on the use of radiation in these patients. This study aims to investigate the role of adjuvant radiation and identify predictors of functional outcome at last follow-up in patients with histology-confirmed intramedullary ependymomas.Methods We conducted a retrospective cohort study at a single center with 101 patients with histologically confirmed grade 2 spine ependymoma. We aimed to identify which patients benefit most from postoperative radiotherapy by analyzing preoperative features and outcomes in adjuvant RT recipients, and to assess functional outcomes at last follow-up. Patients with subependymomas, conus/filum terminale tumors, or drop metastases were excluded. KNN (K-Nearest Neighbors) matching based on age and sex was used to match patients.Results A total of 101 patients were included in this study, with a mean age of 43.2 years. The cervical spine was the most common location of the tumor (68.3%). The cohort had a median follow-up time of 1.09 (0.34–3.31) years. Nine patients received radiation following tumor resection to prevent recurrence. The median total radiation dose was 4680 cGy (range: 4550–5040 cGy), with a median fractionated dose of 180 cGy (range: 180–200 cGy), delivered over an average of 23.7 ± 7.6 days. After matching, 27 patients were in the no-radiation group and 9 in the radiation group, the mean tumor volumes in the no-radiation and radiation groups were 4.0 ± 5.0 cm^3 and 2.8 ± 2.9 cm^3, respectively ($p = 0.558$). Recurrence occurred in two of nine radiation patients and none of the non-radiation patients, with radiation typically reserved for higher-risk clinical scenarios such as residual disease, multiple recurrences, large tumor volume, internal hemorrhage, and subtotal resection. Preoperative symptoms, including pain, sensory symptoms, and weakness, did not differ significantly between the groups ($p > 0.05$). Preoperatively, there were higher number of functionally dependent patients in the radiation group (22.2%) compared to the no-radiation group (11.1%), although this difference was not statistically significant ($p = 0.404$). At last follow-up, weakness was more frequent radiation group (55.6% vs. 11.1%, $p < 0.005$). An exploratory multivariable analysis of the entire cohort revealed postoperative radiation (adj. $p = 0.008$), was associated with weakness at last follow up.Conclusion Our findings highlight the need to consider radiotherapy carefully and tailor its use on a case-by-case basis in patients with grade 2 ependymoma.

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Review > Front Oncol. 2026 Aug 14:16:1874371. doi: 10.3389/fonc.2026.1874371. eCollection 2026.

Centre Eugène Marquis RENNES

Report from the National Pediatric Cancer Foundation – infantile glioma and other non-embryonal central nervous system tumors: evolving molecular advances and current treatment landscape

Evan Cantor [1 2], Haya Qutob [2], Jackson Ayers [2], Brennan Donnville [2], Christian Nieves [3], Valerie Cruz-Flores [4], Stacie Stapleton [4], Neha J Patel [5]

Affiliations + expand

PMID: 42666540 PMCID: PMC13523012 DOI: 10.3389/fonc.2026.1874371

Background: Brain tumors in infants represent a rare but clinically challenging subset of pediatric central nervous system (CNS) neoplasms. These tumors are biologically and clinically distinct from those in older children and adults, with a predilection for supratentorial locations, frequent presentation with macrocephaly and signs of increased intracranial pressure, and unique molecular profiles. There have been many advances in molecular profiling, now influencing treatment choice and outcomes. Non-embryonal tumor types-including glial tumors, choroid plexus tumors, craniopharyngioma, ependymoma, teratoma, and germ cell tumors-collectively constitute the majority of infant brain tumors and warrant focused attention.

Methods and scope: This review synthesizes the current literature on the epidemiology, molecular biology, clinical presentation, management, and outcomes of non-embryonal brain tumors diagnosed in infants (age ≤12-36 months). Tumor types addressed include low-grade and high-grade gliomas (including the recently defined infant-type hemispheric glioma [IHG]), choroid plexus papilloma and carcinoma, ependymoma, craniopharyngioma, teratoma, and intracranial germ cell tumors.

Key findings: Glial tumors are among the most common infant brain tumors, with low-grade gliomas demonstrating excellent survival approaching 100%, while high-grade gliomas carry a significantly worse prognosis. IHGs are a molecularly distinct entity driven by receptor tyrosine kinase (RTK) fusions involving ALK, NTRK1/2/3, ROS1, and MET, with three-year overall survival of approximately 80% and emerging evidence supporting targeted tyrosine kinase inhibitor therapy. Choroid plexus papillomas peak during infancy and are curable with gross total resection, whereas choroid plexus carcinomas have five-year survival rates of 61-65% and require multimodal therapy. Posterior fossa A (PFA) ependymomas predominate in infants and behave more aggressively than other ependymoma subtypes. Craniopharyngiomas, though rare in infancy, present unique surgical challenges given their proximity to the hypothalamic-pituitary axis. Intracranial teratomas are the most common congenital brain tumors.

Conclusions: Non-embryonal infant brain tumors encompass a heterogeneous group of neoplasms with widely variable outcomes. Advances in molecular classification-particularly the identification of targetable RTK fusions in IHG-are reshaping therapeutic paradigms. Integrated histopathologic and molecular characterization per the WHO CNS5 classification is essential for accurate diagnosis and optimal treatment planning in this vulnerable population. Collaborative, prospective studies are needed to establish standardized treatment approaches and improve long-term neurocognitive outcomes.

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Surgical outcomes and prognostic factors in epilepsy associated with **low-grade** brain tumors: a systematic review.

Reyes JS, Leal SI, Estupiñan-Pepinosa DF, Correa-Molina N, Niño-Muñoz PA, Navarro-Ramirez LM, Aguirre-Patiño JS.

Neurosurg Rev. 2026 Feb 13;49(1):221. doi: 10.1007/s10143-026-04140-0.

Low-grade brain tumors such as gangliogliomas (GGs) and dysembryoplastic neuroepithelial tumors (DNETs) are common causes of drug-resistant epilepsy, particularly in children and young adults. While surgery is widely used to achieve seizure control, the degree of benefit and prognostic factors remain variably reported across the literature. To systematically evaluate seizure outcomes, extent of resection, and recurrence rates in patients undergoing epilepsy surgery for low-grade brain tumors. We conducted a systematic review of PubMed, Scopus, and Web of Science, following PRISMA 2020 guidelines. Sixty-seven studies involving 4,314 patients met inclusion criteria. Detailed characteristics of all included studies, including outcome definitions, follow-up duration, and key confounders, are provided in Table 2. Data on tumor type, extent of resection, seizure outcomes using Engel or International League Against Epilepsy (ILAE) classifications, recurrence, and complications were extracted. Risk of bias was assessed using the Newcastle–Ottawa Scale. Seizure freedom (Engel Class I or ILAE 1) was frequently reported, with rates often exceeding 70% across studies, with representative cohorts reporting rates of 215/287 at 60 months, 48/51 at a mean 44.2 months, and 20/26 at a mean 49.7 months. Gross total resection (GTR) was often associated with higher reported seizure freedom compared to subtotal resection, although stratified denominators were inconsistently reported across studies. GGs and DNETs showed the most favorable outcomes. Tumor recurrence was infrequently reported, particularly in patients with GTR. Postoperative morbidity was low, with only isolated cases of transient neurological deficits. Epilepsy surgery outcomes are particularly favorable for GGs and DNETs, especially when Gross Total Resection is achieved. Early intervention is associated with better outcomes, and surgery should be considered an early therapeutic option in appropriately selected patients with drug-resistant epilepsy and circumscribed lesions. Standardized reporting and prospective studies are needed to optimize surgical strategies and long-term care.

Stereotactic radiosurgery for residual rosette-forming **glioneuronal tumor**: a case report and literature review.

Hsiao YL, Yang HC, Lin CF, Lee CC, Liou KD, Peng TC.

Acta Neurochir (Wien). 2026 Feb 2;168(1):26. doi: 10.1007/s00701-026-06773-y.

Introduction and importance: Rosette-forming glioneuronal tumor (RGNT) is a rare World Health Organization grade I tumor of the central nervous system, most commonly found in the fourth ventricle. Preoperative diagnosis is challenging, and optimal management for incompletely resected tumors is not well-established.

Case presentation: An 8-year-old boy presented with headaches and declining vision due to obstructive hydrocephalus caused by a large fourth ventricle tumor with extension into the cerebellopontine angle. After an endoscopic third ventriculostomy, the patient underwent maximal safe subtotal resection. Histopathological examination confirmed RGNT. Given the residual tumor, adjuvant radiotherapy was administered. Following treatment, the patient's symptoms resolved, and follow-up imaging demonstrated stable residual disease.

Clinical discussion: Although RGNTs are indolent tumors, their location in the fourth ventricle often precludes complete resection. Subtotal resection followed by adjuvant radiotherapy *may represent a valid option in selected cases* where complete resection is not feasible, with the aim of balancing tumor control and neurological preservation. This case adds to the limited pediatric experience and emphasizes the importance of a personalized, multidisciplinary approach with careful long-term surveillance.

Conclusion: This case highlights the importance of *individualized, multidisciplinary decision-making* in the management of pediatric RGNTs of the fourth ventricle when complete resection is not feasible.

TGN

Disseminated Rosette Forming **Glioneuronal Tumor**- A Rare Presentation with Review of Literature.

Khanna G, Yadav A, Gupta S, Singla T, Gupta M.

Neurol India. 2026 Jul 1;74(4):684-687. doi: 10.4103/neurol-india.Neurol-India-D-25-00638. Epub 2026 Jul 21.

Multifocal rosette-forming **glioneuronal tumor**-like low-grade **glioneuronal tumor** with dysembryoplastic neuroepithelial tumor features associated with drug-resistant epilepsy: a case report and literature review.

Ishida Y, Ise K, Sato K, Asanome T, Yoshihara R, Aburakawa Y, Izumi M, Oda Y, Sugino H, Tanei ZI, Tsuda M, Tanaka S.

Brain Tumor Pathol. 2026 Jan 6. doi: 10.1007/s10014-025-00526-y. Online ahead of print.

Myxoid **glioneuronal tumor** with PDGFRA p.K385 mutation: Radiological insights from two cases.

Zeng A, Su X, Hu W, Yue Q.

Neurocirugia (Engl Ed). 2026 Mar-Apr;37(2):500725. doi: 10.1016/j.neucie.2025.500725. Epub 2025 Nov 21.

SLC44A1::PRKCA fusion-positive **glioneuronal tumor** without histological and epigenetic features of papillary **glioneuronal tumor**.

Huynh V, Zhang D, Raghunathan A, Hardcastle J, Smoley S, Isaacson M, Gandham M, Dasari S, Abdullaev Z, Aldape K, Quezado M, Pratt D, Cimino PJ, Lachance D, Ida CM.

J Neuropathol Exp Neurol. 2026 Jul 1;85(7):797-800. doi: 10.1093/jnen/nlaf133.

Myxoid **glioneuronal tumor** of the septum pellucidum with concurrent dual PDGFRA and FGFR3 gene mutations: a case report and literature review.

Wang M, Wang L, Zhang L, Zhang J, Yang Y, Zhang L.

Front Oncol. 2026 Sep 1;16:1903894. doi: 10.3389/fonc.2026.1903894. eCollection 2026.

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ONC206 demonstrates potent antitumorigenic activity and is a potential novel therapeutic strategy for high-risk medulloblastoma.

Tzaridis T, Liu J, Chien FL, Malhotra A, Zhu D, Gershon I, Zhang H, Velazquez Vega JE, Schniederjan M, Sposito T, Adams PD, Allen JE, Prabhu VV, Wechsler-Reya RJ, MacDonald TJ.

Neuro Oncol. 2026 Jul 1;28(7):1753-1768. doi: 10.1093/neuonc/noag053.

Background: Medulloblastoma (MB) is the most common malignant pediatric brain tumor, and has an urgent need for novel treatment approaches. Dordaviprone (ONC201) and its chemical derivative with nanomolar potency, ONC206, induce apoptosis of cancer cells by activation of the mitochondrial caseinolytic protease P (ClpP). Dordaviprone is currently in phase I clinical trials for pediatric patients with primary brain tumors.

Methods: In this study, we evaluated the preclinical therapeutic effects of ONC206 in MB and investigated its mechanism of action.

Results: We found evidence for high expression of ClpP at both the RNA and protein level in MB tumors, compared to very low expression in normal brain tissue. In addition, we saw a pronounced reduction in cell viability of human group 3 and group 4 and murine Sonic-Hedgehog-activated (SHH)-driven and group 3 MB cells treated with ONC206 with low IC-50s. After treatment with ONC206, we observed an induction of integrated stress response and mitochondrial damage. To test the efficacy of ONC206 in vivo, we used murine models of SHH-driven and group 3 MB as well as group 3 and group 4 patient-derived xenografts (PDXs). Dordaviprone led to a significant prolongation of survival in both murine models, with the SHH mice demonstrating survival extension from 70 to 140 days. Patient-derived xenograft-bearing mice also responded to ONC206, which led to a significant survival benefit.

Conclusion: Our results highlight ONC206 as a novel therapeutic option for patients with high-risk MB and provide strong rationale for testing the efficacy of ONC206 in the treatment of these patients.

High-dose chemotherapy and craniospinal irradiation-sparing approach for WNT medulloblastoma of early childhood.

Nobre L, Ramaswamy V, Coleman C, Dhall G, Senapati A, Toledano H, Jabado N, Bouffet E, Lafay-Cousin L.

J Neurooncol. 2026 Jan 19;176(3):172. doi: 10.1007/s11060-026-05425-6.

BACKGROUND: Adjuvant chemotherapy and craniospinal irradiation led to excellent survival in older children (≥ 3 years) with WNT medulloblastoma, allowing for ongoing careful treatment de-escalation. However, treatment with standard dose chemotherapy alone or in combination with involved field radiotherapy to the tumor bed only had high rates of distant treatment failure. In younger children, WNT medulloblastomas are extremely rare and the survival following high-dose chemotherapy (HDC) and radiation-sparing strategies has not been reported. PATIENTS AND METHODS: Through international collaboration, we assembled a cohort of young children with WNT medulloblastoma treated with HDC and craniospinal irradiation avoidance to describe their survival and neurocognitive and ototoxicity profile. RESULTS: Five patients, diagnosed at median age of 7.0 years (range 2.7–7.5) underwent HDC and autologous stem cell transplantation. None of them received adjuvant radiotherapy. All patients were alive beyond four years from diagnosis. Evaluated patients had neurocognitive abilities reported within low average to average range. CONCLUSION: In this cohort, the survival of young children with WNT MB treated with HDC alone was excellent. The rare possibility of a molecular diagnosis of WNT MB in early childhood should not be viewed as an exclusion criterion to enroll on infant brain tumor strategies relying on HDC consolidation. CLINICAL TRIAL NUMBER: Not applicable.

Late Effects in Survivors of Pediatric **Medulloblastoma**: A Comprehensive **Review**.

Izurieta-Pacheco AC, Ramaswamy V, Tsang DS, Rutka J, Wasserman J, Guger S, Weidman DR, Nathan PC, Scheinemann K, Bennett J.

Pediatr Blood Cancer. 2026 Jan;73(1):e32132. doi: 10.1002/pbc.32132. Epub 2025 Oct 30.

Medulloblastoma (MB) treatment has advanced significantly with the integration of molecular subgrouping, enabling more precise risk stratification and tailored therapies. While survival outcomes have improved, long-term treatment-related morbidity remains a significant challenge. This review summarizes the spectrum of late effects experienced by survivors of pediatric MB. Special attention is placed on the impact of proton therapy in reducing treatment toxicity. As therapeutic paradigms continue to evolve, historical data may no longer accurately reflect the toxicity profile of contemporary treatments. Therefore, prospective, molecularly annotated survivorship studies are needed to determine whether recent advances in treatment will lead to sustained improvements in health, functionality, and quality of life.

Outcomes of immunotherapy in **medulloblastoma**: a systematic **review**.

Fontão P, Viana-Pereira M, Pinto-Ribeiro F, Junqueira T, Reis RM.

Oncologist. 2026 May 8;31(6):oyag109. doi: 10.1093/oncolo/oyag109.

Background: Medulloblastoma is the most common malignant brain tumor in children. Medulloblastoma has intrinsic characteristics that pose significant challenges to effective immunotherapy. Nevertheless, several clinical trials have explored immunotherapeutic strategies in patients diagnosed with medulloblastoma. This systematic review aimed to synthesize all immunotherapy modalities investigated in medulloblastoma patients and reported clinical outcomes.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, and ClinicalTrials.gov from inception to 30 June 2025 using the terms "immunotherapy" and ("brain tumor," "pediatric brain tumor," or "medulloblastoma"). Original articles, clinical trials, and conference abstracts evaluating any immunotherapeutic intervention in patients with medulloblastoma were included. Risk of bias was assessed using JBI critical appraisal tools.

Results: Fifty-six studies met the inclusion criteria, encompassing at least 183 patients with medulloblastoma. Nearly half were Phase I trials (24/56, 43%), and 18% (10/56) were non-trial designs. Among the 29 studies reporting clinical outcomes, adoptive cellular therapies in combination regimens (7/29, 24%) and immune checkpoint inhibitors (6/29, 21%) were most frequently evaluated. Overall, clinical benefit was limited. Median overall survival ranged from 1.29 to 47 months, and median progression-free survival from 0.79 to 11 months. Progressive disease was reported in 40 patients, partial responses in 13, and complete responses in three patients.

Conclusions: Despite increasing trial activity, immunotherapy has shown modest efficacy in patients with medulloblastoma. Interpretation is limited by small cohorts, heterogeneity, and inconsistent reporting of outcomes. Future studies should prioritize rational antigen selection, molecular subgroup stratification, and improved trial design.

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- METASTASES CEREBRALES
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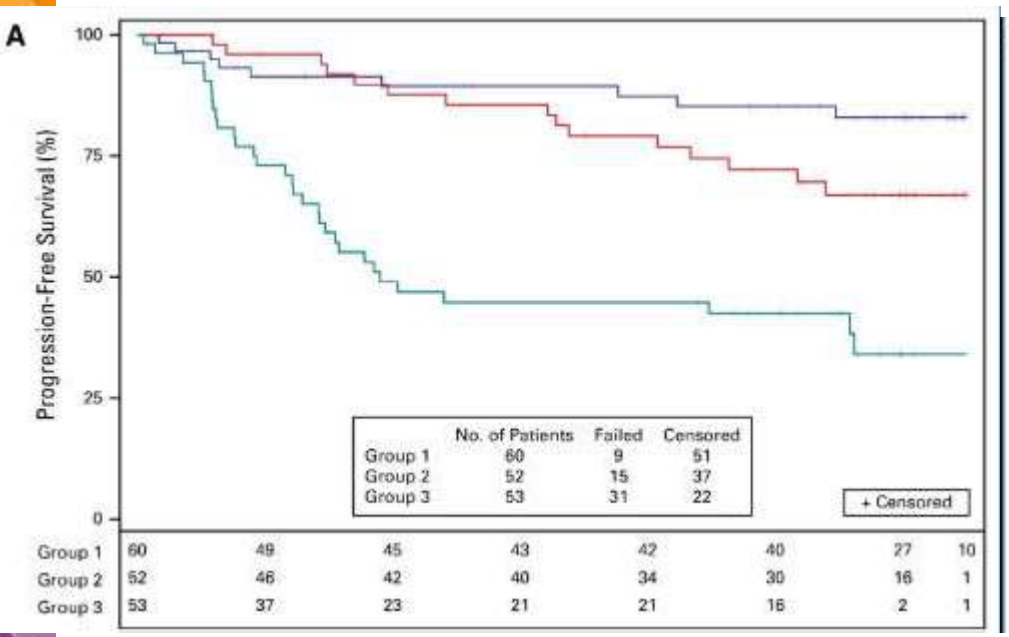
Centre Eugène Marquis RENNES

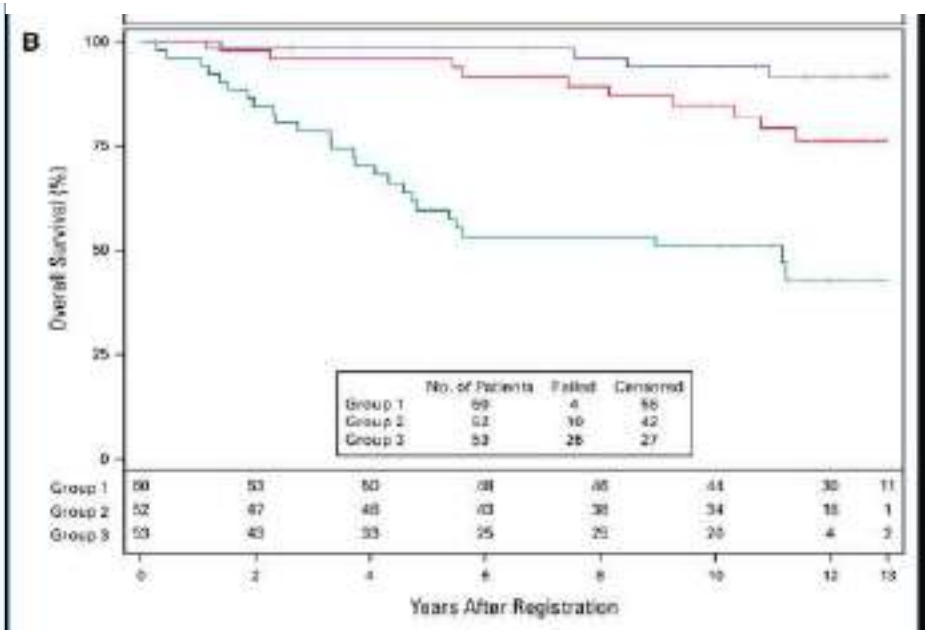
Long-Term Analysis of NRG Oncology RTOG 0539: A Phase II **Trial** of Observation for Low-Risk **Meningioma** and Radiotherapy for Intermediate- and High-Risk **Meningioma**.

Kotecha R, Polley MY, Vogelbaum MA, Perry A, Ashby L, Modi JM, Alleman AM, Tsien CI, Barani IJ, Li J, Braunstein S, Whitton AC, Bovi JA, Deb N, Lindhorst SM, Shrieve DC, Robinson CG, Shu HG, Vempati P, Mishra MV, Suh JH, Bloom B, Hunter GK, Won M, Mehta MP, Rogers CL.

J Clin Oncol. 2026 Aug 10;44(23):2169-2175. doi: 10.1200/JCO-25-01441. Epub 2026 May 27.

NRG Oncology RTOG 0539 was a prospective phase II trial of risk-adapted radiotherapy for patients with WHO grade 1-3 meningioma. Low-risk (group 1, n = 60) was defined as a grade 1 tumor after gross total resection or subtotal resection (GTR/STR) and prospectively monitored. Intermediate-risk (group 2, n = 52) was defined as recurrent grade 1 or newly diagnosed grade 2 tumor after GTR and treated with radiotherapy (54 Gy). High-risk (group 3, n = 53) included a newly diagnosed grade 2 tumor after STR, newly diagnosed grade 3 tumor, or recurrent grade 2 or 3 tumor and treated with radiotherapy (60 Gy). Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method. The median follow-up times for the low-, intermediate-, and high-risk cohorts were 12.1, 12.0, and 11.1 years, respectively. The 10-year PFS and OS rates for the low-, intermediate-, and high-risk cohorts were 85.2% and 94.1%, 72.2% and 84.7%, and 42.5% and 51.1%, respectively. Five patients (9.6%) and eight patients (15.1%) had a grade 3+ toxicity attributed to radiotherapy in the intermediate- and high-risk cohorts, respectively. The long-term outcomes using this risk-adapted approach support observation for low-risk patients, inform radiotherapy patient selection and practice standards for intermediate- and high-risk patients, and provide comparative benchmarks for future trials.





In summary, long-term results from RTOG 0539 validate risk-adapted meningioma patient management and provide valuable insights into the outcomes with surveillance for grade 1 meningioma after resection as well as with radiotherapy for relapsed grade 1-3 meningioma or upfront grade 2-3 meningioma following resection. These results should guide current clinical practice and provide a benchmark for future trials.

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Survival and prognostic factors of anaplastic **hemangiopericytoma**/solitary fibrous tumor grade III.

Pando A, Patel AM, Valdivia DJ, Daut CT, Levin-Carrion Y, Shah V, Desai A, Patel P, Eloy JA, Liu JK, Sherman JH.

Acta Neurochir (Wien). 2026 Mar 27;168(1):90. doi: 10.1007/s00701-026-06843-1.

PMID: 41896408 Free PMC article.

Pancreatic Metastasis from Intracranial Solitary Fibrous Tumor/**Hemangiopericytoma** Mimicking a Pancreatic Neuroendocrine Tumor: A Case Report and Focused Literature Review.

Kong X, Tong F, Liu Y, Tang H, Sha H, Du J.

Curr Oncol. 2026 May 29;33(6):323. doi: 10.3390/curroncol33060323.

PMID: 42346223 Free PMC article. Review.

Pediatric orbital solitary fibrous tumor/**hemangiopericytoma** presenting with isolated eyelid edema: a case report.

Gai C, Zhang L, Zhao X, Wang B.

Front Pediatr. 2026 Aug 26;14:1884656. doi: 10.3389/fped.2026.1884656. eCollection 2026.

PMID: 42718733 Free PMC article.

Pediatric intracranial high-grade solitary fibrous tumor/**hemangiopericytoma** with drop metastasis to cervicodorsal spine: a rare case report.

Javaid MH, Shah S, Javed G, Khalid M, Mushtaq RR, Mahmood I.

Int J Surg Case Rep. 2026 Feb 16;138(3):625-631. doi: 10.1097/RC9.0000000000000224. eCollection 2026 Mar.

PMID: 41836984 Free PMC article.

Pulmonary Metastases from a **Hemangiopericytoma**/Solitary Fibrous Tumor Spectrum Neoplasm in a Patient with a Poorly Documented Thigh Tumor: A Case Report.

Dragomir JA, Stoichiță A, Vlăsceanu SG, Matache R, Mahler B.

Reports (MDPI). 2026 Aug 16;9(3):274. doi: 10.3390/reports9030274.

PMID: 42647318 Free PMC article.

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METASTASES CEREBRALES

A phase II study of atezolizumab in combination with stereotactic radiation for patients with triple-negative breast cancer and **brain metastasis**.

Giordano A, Graham N, Aizer AA, Tayob N, Pereslete AM, Schoenfeld JD, Leone JP, Davis R, Erick TK, Mayer EL, Winer EP, Krop I, Tolaney SM, Lin NU.

Breast Cancer Res Treat. 2026 Mar 7;216(2):24. doi: 10.1007/s10549-026-07932-6.

Phase II Efficacy and Safety of Pembrolizumab with Platinum Based Chemotherapy in Non-Small Cell Lung Cancer Patients with Untreated, Asymptomatic **Brain Metastasis** (PHOEBS).

Kim J, Han M, Kim J, Park S, Jung HA, Sun JM, Lee SH, Ahn JS, Shin SH, Lee K, Um SW, Ahn MJ.

Cancer Res Treat. 2026 Mar 19. doi: 10.4143/crt.2025.1100. Online ahead of print.

Molecular and Clinicopathological Biomarkers Predicting **Brain Metastasis** in Triple-Negative Breast Cancer: A Systematic Review.

Agarwal S, Mehranpour P, Chawla A, Vaish C, Han S, Yang I, Wadehra M.

Int J Mol Sci. 2026 Feb 16;27(4):1909. doi: 10.3390/ijms27041909.

A phase II study of atezolizumab in combination with stereotactic radiation for patients with triple-negative breast cancer and **brain metastasis**.

Giordano A, Graham N, Aizer AA, Tayob N, Pereslete AM, Schoenfeld JD, Leone JP, Davis R, Erick TK, Mayer EL, Winer EP, Krop I, Tolaney SM, Lin NU.

Breast Cancer Res Treat. 2026 Mar 7;216(2):24. doi: 10.1007/s10549-026-07932-6.

Purpose: Triple-negative breast cancer (TNBC) patients with brain metastases have a poor prognosis and limited treatment options. Preclinical and clinical evidence suggests that radiotherapy may act synergistically with immune checkpoint inhibitors.

Methods: We conducted an open-label, single-arm, phase II study of atezolizumab plus stereotactic radiosurgery (SRS) in metastatic TNBC patients with brain metastases. The primary endpoint was progression-free survival (PFS) according to the Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) bi-compartmental model. Secondary endpoints included extracranial objective response rate, overall survival (OS), and safety and tolerability. A safety run-in analysis for dose-limiting toxicity (DLT) was performed after the first 6 patients were enrolled and completed the assessment period.

Results: Six patients were enrolled into the safety run-in phase between May 11, 2018 and October 24, 2019. No DLTs were observed, but the study was closed early due to slow accrual. Patients received a median of 2 atezolizumab cycles (range: 2-16), and SRS was administered to all 6 patients. Treatment-related adverse events (TRAEs) occurred in 4 participants (66.7%); all events were grade 2. The median bi-compartmental PFS was 1.3 months (95% confidence interval (CI): 0.95 - NA) and the median OS was 9.7 months (95% CI: 3.6 - NA). The best observed response by RECIST 1.1 criteria was stable disease ≥ 24 weeks in one participant (16.7%).

Conclusions: Concurrent SRS with atezolizumab was feasible in TNBC patients with brain metastases. However, disease outcomes were poor, and the development of effective therapies for these patients remains a significant unmet medical need.

Phase II Efficacy and Safety of Pembrolizumab with Platinum Based Chemotherapy in Non-Small Cell Lung Cancer Patients with Untreated, Asymptomatic **Brain Metastasis** (PHOEBS).

Kim J, Han M, Kim J, Park S, Jung HA, Sun JM, Lee SH, Ahn JS, Shin SH, Lee K, Um SW, Ahn MJ.

Cancer Res Treat. 2026 Mar 19. doi: 10.4143/crt.2025.1100. Online ahead of print.

Purpose: Brain metastases are a serious complication in non-small cell lung cancer (NSCLC). However, data regarding efficacy of immune checkpoint inhibitors and chemotherapy combinations are limited. This phase II study aimed to evaluate the intracranial efficacy and safety of pembrolizumab and chemotherapy in treatment-naïve NSCLC patients with asymptomatic brain metastases.

Materials and methods: This single-arm, phase II trial was conducted at Samsung Medical Center, Korea. Eligible patients had stage IV NSCLC with asymptomatic, untreated brain metastases and no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) alterations. Patients received pembrolizumab with chemotherapy every 3 weeks for 4 cycles, followed by pembrolizumab with or without maintenance chemotherapy up to 35 cycles. The primary endpoint was intracranial objective response rate (icORR). Secondary endpoints included intracranial progression free survival (icPFS), intracranial duration of response (icDoR), objective response rate (ORR), progression free survival (PFS), overall survival, and safety.

Results: Between February 2021 and June 2024, a total of 13 patients were enrolled. Due to challenges in recruiting patients, enrollment was discontinued after the 13 patients. The icORR was 46.2% (95% CI, 19.2-74.8), with 6 patients achieving partial response. The median icPFS was 9.8 months (95% CI, 5.2-21.5), and median icDoR was 9.3 months (95% CI, 4.0-20.3). Median PFS and overall survival was 7.2 months (95% CI, 2.4-12.3) and 10.7 months (95% CI, 7.2-21.5), respectively. Most treatment-related adverse events were grade 1-2."

Conclusion: Pembrolizumab combined with chemotherapy demonstrated encouraging intracranial activity and manageable safety profile in NSCLC patients with untreated, asymptomatic brain metastases.

Molecular and Clinicopathological Biomarkers Predicting **Brain Metastasis** in Triple-Negative Breast Cancer: A Systematic Review.

Agarwal S, Mehranpour P, Chawla A, Vaish C, Han S, Yang I, Wadehra M.

Int J Mol Sci. 2026 Feb 16;27(4):1909. doi: 10.3390/ijms27041909.

Almost half of patients with triple-negative breast cancer (TNBC) develop brain metastasis (TNBCBM), a marker of poor prognosis. TNBC is a more aggressive breast cancer subtype which lacks ER, PR, and HER2 expression, and thus, exploring predictive biomarkers is crucial to improving TNBCBM outcomes through targeted therapy. To curate these biomarkers, peer-reviewed publications from 2010 to 2025 were extracted from PubMed, Scopus, Embase, Cochrane, and Web of Science if they evaluated clinicopathological biomarkers of TNBCBM. A total of 130 studies (60 clinical and 70 pre-clinical) were included. Publications most often featured transcriptomic studies, growth factor receptors, and immune microenvironment markers with 37, 19, and 17 studies identified, respectively. While TNBC aggressiveness has been linked to metastasis, advancing stage, and poor prognosis, several studies focused on utilizing circulating protein and transcriptomic biomarkers for early detection. While few pathways appeared specifically for TNBCBM, investigating these biomarkers further may allow for improved risk stratification, clinical trial design, patient selection, and therapeutic development. Identification of the most promising biomarkers will pave the way for improved prognosis of the most lethal complications of TNBC.

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SCHWANNOME VESTIBULAIRE

Vestibular schwannoma: genetic and epigenetic mechanisms, hearing loss, and emerging therapies.

Otaner F, Himic V, Vargas LO, Abikenari M, Pandey N, Sivanathan S, Kalmanson O, Govindan A, Jung D, Estevez-Ordonez D, Wang A, Jeyaretna S, Shah AH, Komotar RJ, Gampel B, Dinh C, Ivan ME.

J Neurooncol. 2026 May 16;178(1):3. doi: 10.1007/s11060-026-05621-4.

Socioeconomic disparities in **vestibular schwannoma** diagnosis and management: A systematic **review**.

Lally AR, Welch RL, Terraciano A, Vadset T, Saidpour S, Rayden R, Cohen E, Choi A, Berlas S, Bhatta M, Ghosh SR, Agarwal V.

Neurosurg Rev. 2026 Sep 22;49(1):580. doi: 10.1007/s10143-026-04478-5.

MRI-Based Prediction of **Vestibular Schwannoma**: Systematic **Review**.

Yang C, Alvarado D, Ravindran PK, Keizer ME, Hovinga K, Broen MPG, Kunst HPM, Temel Y.

Cancers (Basel). 2026 Jan 17;18(2):289. doi: 10.3390/cancers18020289.

Long-term hearing and facial nerve outcomes after hearing preservation surgery for **vestibular schwannoma**: a systematic **review** and meta-analysis.

Foo JQX, Zheng Y, Hwang PYK.

Neurosurg Rev. 2026 Jan 3;49(1):100. doi: 10.1007/s10143-025-04036-5.

Health-related quality of life in patients with **vestibular schwannoma** managed with observation, stereotactic radiosurgery or microsurgery: a systematic **review** and single-arm meta-analysis.

Pruijn IMJ, Welie FRLM, Kievit W, Kunst HPM.

J Neurol. 2026 Mar 7;273(3):187. doi: 10.1007/s00415-026-13730-3.

A **review** of targeted therapies for NF2-related **vestibular schwannoma**: molecular pathogenesis, emerging therapeutics, and future clinical horizons.

Sokol MK, Ha JH, Li G, Kim LH.

J Neurooncol. 2026 May 16;178(1):1. doi: 10.1007/s11060-026-05599-z.

Merci de votre attention