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RESEARCH

Efficacy of chemoradiotherapy in pediatric H3K27M-mutant diffuse intrinsic pontine glioma: a study based on single-center and SEER data

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Abstract

Background H3K27M-mutant diffuse intrinsic pontine glioma (DIPG) is a lethal pediatric brainstem tumor with a median overall survival (OS) of less than one year. Radiotherapy (RT) is the standard treatment, but the survival benefit of adding temozolomide (TMZ) remains controversial.

Methods Two retrospective cohorts were analyzed. In the single-center cohort (44 patients), patients were divided into three groups: RT alone ($n=16$), Stupp regimen (concurrent and adjuvant TMZ, $n=15$), and RT followed by sequential TMZ (RT→TMZ, $n=13$). In the SEER database cohort (39 patients), patients were divided into RT alone ($n=19$) and chemoradiotherapy (CRT, $n=20$). Survival was analyzed using the Kaplan-Meier method, log-rank test, and Cox regression.

Results In the single-center cohort, no significant differences were observed among the three groups in objective response rate (ORR; $P=0.693$), disease control rate (DCR; $P=1.000$), median progression-free survival (PFS; 6, 7, and 8 months, respectively; $P=0.621$), or median OS (11, 13, and 13 months, respectively; $P=0.534$). The Stupp group had significantly higher rates of leukopenia and liver function impairment than the RT group ($P<0.05$), with a trend toward more grade≥3 adverse events (AEs). No significant difference in AEs was seen between RT→TMZ and RT. In the SEER cohort, median OS was 11 months in both groups ($P=0.582$); median disease-specific survival (DSS) was 11 and 12 months, respectively ($P=0.585$).

Conclusion Adding TMZ to RT whether (concurrent/adjuvant or sequential) does not significantly improve PFS or OS in H3K27M-mutant DIPG patients. The Stupp regimen significantly increases hematological and hepatic toxicity.

Keywords H3K27M mutation · Diffuse intrinsic pontine glioma · Radiotherapy · Temozolomide · Chemotherapy · SEER database

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Introduction

Diffuse intrinsic pontine glioma (DIPG) is among the most aggressive tumors of the central nervous system in children, characterized by rapid clinical progression and a dismal prognosis [1]. Accounting for approximately 70%–80% of pediatric brainstem tumors, DIPG has an annual incidence of roughly 1.78 per 100,000 in the United States [1, 2]. The tumor diffusely infiltrates the pons, intertwining with critical neural structures, which precludes curative surgical resection [1–3]. The progressive worsening of the classic clinical triad (cranial neuropathies, long tract signs, and cerebellar signs) severely compromises patients' quality of life and portends a poor outcome [1, 2, 4].

Radiotherapy (RT), primarily involving fractionated external beam irradiation, is currently the only established standard of care, providing transient neurological improvement and extending survival [3, 5]. Standard regimens (54–60 Gy, 1.8–2.0 Gy/fraction) lead to symptomatic improvement in over 70% of patients, yielding a median PFS of approximately 6–9 months [5, 6]. However, these benefits are not durable; the vast majority of patients experience recurrence within months, with a median OS of only 9–12 months and a 2-year survival rate below 10% [2, 4, 6].

In 2012, Khuong-Quang et al. first reported that over 70% of DIPG cases harbor mutations in the H3.3 or H3.1 histone genes, leading to the replacement of lysine by methionine at position 27 (H3K27M) [7]. This mutation reduces genome-wide H3K27 trimethylation by inhibiting EZH2, a core subunit of the polycomb repressive complex 2 (PRC2) [8, 9]. This process relieves transcriptional repression of oncogenes, driving proliferation, differentiation arrest, and enhancing resistance to chemoradiotherapy [8–10]. Given its clear pathogenic role and prognostic significance, the 2016 WHO Classification of Tumors of the Central Nervous System established "diffuse midline glioma, H3K27M-mutant" as a distinct diagnostic entity [10]; the subsequent 2021 fifth edition further refined this to "diffuse midline glioma, H3 K27-altered" (WHO grade 4) [11]. The H3K27M mutation has thus become a key molecular stratification marker for DIPG.

Therapeutically, drawing from experience in adult glioblastoma, regimens combining radiotherapy with TMZ have been extensively explored [12, 13]. However, given the fundamental differences in molecular background and biology between DIPG and adult glioblastoma, the efficacy of TMZ remains highly controversial [3, 14]. Several prospective clinical trials have demonstrated that adding concurrent/adjuvant TMZ to radiotherapy fails to significantly improve survival outcomes in pediatric high-grade glioma or DIPG [15–17]. Conversely, some retrospective studies have suggested potential benefit in specific subgroups, showing a trend toward improved OS [18, 19]. These conflicting results may stem from heterogeneity in patient populations, differences in the timing of chemotherapy administration (concurrent vs. sequential), and confounding bias introduced by the lack of H3K27M molecular stratification in earlier studies [20]. Therefore, a reassessment of TMZ's value in a more homogeneous population, specifically within H3K27M-mutant DIPG, is warranted.

The current understanding is predominantly based on data from Western populations, with a notable lack of systematic research in Chinese cohorts. Considering China's large pediatric population, conducting studies based on domestic patients is not only an urgent need to optimize clinical practice but also a crucial contribution to complementing the global body of evidence.

This study was a retrospective, non-randomized, observational cohort study that integrated real-world data from a single-center cohort in China with cases from the US SEER database [21], focusing on pediatric patients with pathologically confirmed H3K27M-mutant DIPG. Our objectives were twofold: (1) to systematically compare differences in short-term efficacy, long-term survival, and safety profiles among three treatment modalities—radiotherapy alone, radiotherapy with concurrent and adjuvant TMZ (Stupp regimen), and radiotherapy followed by sequential TMZ-within the single-center cohort; and (2) to leverage the SEER database for external validation, assessing the generalizability of any survival benefit associated with chemoradiotherapy in a broader population.

Materials and methods

Study population

Single-center cohort

A total of 44 consecutive pediatric patients (< 18 years of age) with pathologically confirmed H3K27M-mutant DIPG who received standard radiotherapy at our hospital between January 2018 and January 2025 were enrolled. Treatment regimens were selected by the attending physicians based on patient performance status, family preferences, and institutional practice. Due to the long study period (2018–2025), temporal trends were observed: RT alone and sequential RT→TMZ were mainly used before 2021, while the Stupp regimen was increasingly used after 2021. The study was approved by the hospital's Ethics Committee (Approval No. L/G2022-K001-003) and complied with the principles of the Declaration of Helsinki.

SEER database cohort

Pediatric patients (< 18 years of age) with pathologically confirmed H3K27M-mutant DIPG (ICD-O-3:9385/3) who received radiotherapy were extracted from the SEER database (Incidence-SEER Research Data, 17 Registries, Nov 2024 Sub, 2000–2022). A total of 39 patients were identified. Because the data are de-identified, the study was exempt from institutional ethics review.

Inclusion and Exclusion Criteria

Single-center cohort

Inclusion criteria: (1) Pathological confirmation: positive immunohistochemical staining for H3K27M mutant protein; (2) Age < 18 years; (3) Received standard radiotherapy (54–60 Gy in 30–33 fractions, 1.8–2.0 Gy per fraction); (4) Complete clinical and follow-up data available.

Exclusion criteria: (1) History of another malignancy; (2) Any prior anti-tumor treatment before radiotherapy; (3) Missing key data; (4) Presence of severe non-neoplastic comorbidity; (5) Treatment regimen that did not conform to the predefined study groups.

SEER Cohort

Inclusion criteria: (1) Age < 18 years; (2) ICD-O-3: 9385/3; (3) Radiotherapy recorded as "Beam radiation"; (4) Pathological confirmation by biopsy or surgery.

Exclusion criteria: (1) Lack of pathological confirmation; (2) Missing survival time or status; (3) Unclear cause of death classification.

Grouping and treatment regimens

Grouping in the single-center cohort

Patients were divided into three groups according to the actual treatment received:

1. Radiotherapy alone (RT, n=16): Received standard radiotherapy only.
2. Stupp regimen (Stupp, n=15): The standard Stupp regimen was administered. During the concomitant phase, TMZ was given orally at a daily dose of 75 mg/m^2 starting from the first day of RT and continued until the end of RT. After a 4-week rest period, patients proceeded to the adjuvant phase. The adjuvant phase consisted of 28-day cycles, with TMZ taken orally once daily for the first 5 days of each cycle. The dose was 150 mg/m^2/day in cycle 1 and was escalated to 200 mg/m^2/day from cycle 2 onward, for a total of 6 cycles or until disease progression [13].
3. Radiotherapy followed by sequential TMZ (RT→TMZ, n=13): Adjuvant TMZ was initiated 4 weeks after the completion of radiotherapy. The chemotherapy regimen was identical to the adjuvant phase of the Stupp group: 28-day cycles, with oral administration once daily for 5 consecutive days. The dose was 150 mg/m^2/day in cycle 1 and increased to 200 mg/m^2/day from cycle 2 onward, for a total of 6 cycles or until disease progression.

Grouping in the SEER cohort

Based on treatment records, patients were divided into: (1) Radiotherapy alone (RT, $n = 19$) and (2) Chemoradiotherapy (CRT, $n = 20$): received radiotherapy plus chemotherapy (specific details unavailable).

Data collection and follow-up

Single-center cohort

Data were collected from the medical record system and by telephone follow-up, with a cut-off date of December 1, 2025. Baseline information included age, sex, Lansky performance score, symptoms, maximum tumor diameter, Ki-67 index, P53 expression, and surgical procedure. Tumor size was measured as the maximum axial diameter (in mm) on axial MRI sequences. Response assessment was performed using the RANO criteria [22]. The ORR was defined as the proportion of patients achieving complete response (CR) or partial response (PR), and the DCR was defined as the proportion achieving CR, PR, or stable disease (SD). PFS was defined as the time from diagnosis to radiographic progression or death. OS was defined as the time from diagnosis to death from any cause. AEs were graded according to CTCAE version 5.0 [23].

SEER cohort

Data on age, sex, race, tumor size, surgery, radiotherapy, chemotherapy, survival time, survival status, and cause of death were extracted using SEER*Stat. Tumor size in the SEER database was extracted as the maximum axial diameter (in mm), consistent with the single-center cohort. OS was defined as the time from diagnosis to death from any cause. DSS was defined as the time from diagnosis to death attributable to the disease.

Statistical analysis

All statistical analyses were performed using R software (version 4.5.2; R Core Team, 2025. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/). Categorical variables were compared among groups using the χ^2 test or Fisher's exact test, as appropriate. Survival curves were estimated using the Kaplan-Meier method and compared using the log-rank test. All tests were two-sided, and a P-value <0.05 was considered statistically significant.

Results

Baseline patient characteristics

Single-center cohort

A total of 44 patients were included. No statistically significant differences were observed among the three groups (RT, Stupp, RT→TMZ) regarding baseline characteristics, including age, sex, Lansky Performance Score, symptom types, tumor size, MRI contrast enhancement, P53 expression, and Ki-67 index (all $P>0.05$), confirming inter-group comparability (Table 1).

SEER database cohort

A total of 39 patients were identified. There were no statistically significant differences between the RT and CRT groups in terms of age, sex, race, tumor size, time from diagnosis to treatment, WHO grade, or surgical procedure (all $P>0.05$), establishing baseline comparability between the groups. Detailed baseline data are presented in Supplementary Table S1.

Treatment response analysis in the single-center cohort

The distribution of best overall response did not differ significantly among the three groups ($P=0.937$). For the entire cohort, the ORR was 27.3%, and the DCR was 77.3%. No statistically significant differences were found among the three groups in ORR ($P=0.693$) or DCR ($P=1.000$) (Table 2).

Survival analysis

Single-center cohort

For the entire cohort, the median PFS was 7 months (95% CI: 6.0–8.0), and the median OS was 12 months (95% CI: 11.0–14.0). There were no significant differences among the three groups in median PFS (RT: 6 months, Stupp: 7 months, RT→TMZ: 8 months; $P=0.621$) or median OS (RT: 11 months, Stupp: 13 months, RT→TMZ: 13 months; $P=0.534$) (Fig. 1). Cox regression analysis, using the RT group as the reference, showed no survival benefit for either the Stupp group (PFS: HR = 0.73, 95% CI: 0.34–1.57, $P=0.424$; OS: HR = 0.67, 95% CI: 0.32–1.39, $P=0.282$) or the RT→TMZ group (PFS: HR = 0.74, 95% CI: 0.34–1.61, $P=0.441$; OS: HR = 0.71, 95% CI: 0.33–1.50, $P=0.368$). Detailed Cox regression results for the single-center cohort are provided in Supplementary Tables S2 (PFS) and S3 (OS).

SEER database cohort

For the entire SEER cohort, the median OS was 11 months (95% CI: 9.0–15.0), and the median DSS was 12 months (95% CI: 10.0–16.0). No significant differences were observed between the RT and CRT groups in median OS (both 11 months, $P=0.582$) or median DSS (11 vs. 12 months, $P=0.585$) (Fig. 2). Cox regression analysis confirmed that, compared to the RT group, the CRT group did not have improved OS (HR = 1.22, 95% CI: 0.58–2.57, $P=0.599$) or DSS (HR = 1.23, 95% CI: 0.57–2.66, $P=0.603$). Detailed Cox regression results for the SEER cohort are provided in Supplementary Tables S4 (OS) and S5 (DSS).

Safety analysis in the single-center cohort

Compared to the RT group, the Stupp group exhibited significantly higher incidences of leukopenia (46.7% vs. 6.2%, $P=0.015$), elevated ALT (60.0% vs. 6.2%, $P=0.002$), and elevated AST (53.3% vs. 6.3%, $P=0.006$). Furthermore, there was a trend towards increased rates of grade ≥ 3 AEs (40.0% vs. 12.5%) and nausea/vomiting (86. 7% vs. 62.5%) in the Stupp group. No statistically significant differences in AEs rates were found between the RT→TMZ group and the RT group, although a trend towards higher rates was noted for several parameters (e.g.leukopenia, elevated AST) (Table 3).

Table 1 Baseline characteristics and intergroup comparison of patients in a single center

Characteristic	Treatment				*P*
	Overall (*N*=44)	RT (*N*=16)	Stupp (*N*=15)	RT→TMZ (*N*=13)	
Age, n (%)					0.056
3–10	19 (43.2%)	10 (62.5%)	3 (20.0%)	6 (46.2%)	
11–17	25 (56.8%)	6 (37.5%)	12 (80.0%)	7 (53.8%)	
Sex, n (%)					0.658
Female	23 (52.3%)	7 (43.8%)	9 (60.0%)	7 (53.8%)	
Male	21 (47.7%)	9 (56.3%)	6 (40.0%)	6 (46.2%)	
Lansky, n (%)					0.722
<70	9 (20.5%)	4 (25.0%)	2 (13.3%)	3 (23.1%)	
≥70	35 (79.5%)	12 (75.0%)	13 (86.7%)	10 (76.9%)	
Symptom type, n (%)					0.739
Cranial nerve Palsy	21 (47.7%)	7 (43.8%)	7 (46.7%)	7 (53.8%)	
Cerebellar signs	13 (29.5%)	4 (25.0%)	6 (40.0%)	3 (23.1%)	
Pyramidal signs	10 (22.7%)	5 (31.3%)	2 (13.3%)	3 (23.1%)	
Extra pontine extension, n (%)					0.835
No	12 (27.3%)	4 (25.0%)	5 (33.3%)	3 (23.1%)	
Yes	32 (72.7%)	12 (75.0%)	10 (66.7%)	10 (76.9%)	
Tumor size (mm), **n (%)**					0.964
≤20	12 (27.3%)	4 (25.0%)	5 (33.3%)	3 (23.1%)	
21—40	15(34.1%)	6 (37.5%)	4 (26.7%)	5 (38.5%)	
>40	17 (38.6%)	6 (37.5%)	6 (40.0%)	5 (38.5%)	
MRI enhancement, n (%)					0.461
Yes	7 (15.9%)	2, (12.5%)	4 (26.7%)	1 (7.7%)	
No	37 (84.1%)	14 (87.5%)	11 (73.3%)	12 (92.3%)	
Duration of sympoms at diagnosis(days), n (%)					0.658
≤28	21 (47.7%)	9 (56.3%)	6 (40.0%)	6 (46.2%)	
>28	23 (52.3%)	7 (43.8%)	9 (60.0%)	7 (53.8%)	
P53, n (%)					0.414
Negative	9 (20.5%)	4 (25.0%)	4 (26.7%)	1 (7.7%)	
Positive	35 (79.5%)	12 (75.0%)	11 (73.3%)	12 (92.3%)	
Ki-67, n (%)					>0.999
Low	6, (13.6%)	2, (12.5%)	2, (13.3%)	2, (15.4%)	
High	38 (86.4%)	14 (87.5%)	13, (86.7%)	11, (84.6%)	
Surgery, n (%)					0.675
Biopsy only	24, (54.5%)	10, (62.5%)	8, (53.3%)	6, (46.2%)	
Partial resection	20, (45.5%)	6, (37.5%)	7, (46.7%)	7, (53.8%)	
Bevacizumab after PFS, n (%)					0.631
No	21 (47.7%)	9 (56.3%)	7 (46.7%)	5 (38.5%)	
Yes	23 (52.3%)	7 (43.8%)	8 (53.3%)	8 (61.5%)	

Note: RT: Radiotherapy alone group; Stupp: Radiotherapy combined with concurrent and adjuvant temozolomide chemotherapy group; RT→TMZ: Radiotherapy followed by temozolomide chemotherapy group. Tumor size was measured as the maximum axial diameter on axial MRI sequences. Detailed temozolomide dosing schedules are described in Materials and Methods, Sect. 3.1

Discussion

Although RT remains the standard treatment for pediatric DIPG, the median survival for patients remains less than one year [24]. The discovery of the H3K27M mutation, which defines this tumor as a distinct molecular entity (WHO grade 4) [25, 26], has prompted a re-evaluation of adding TMZ to RT within this molecularly homogeneous population—a strategy successful in adult glioblastoma but long-debated in pediatric DIPG [3, 23, 27]. To address this, we integrated a single-center cohort (n = 44) with a SEER database cohort (n = 39) to assess the efficacy and safety associated with RT ± TMZ.

Our study demonstrates that the addition of TMZ to RT (whether administered concurrently and adjuvantly or sequentially) failed to improve either PFS or OS. This negative finding was highly consistent across two independent, well-balanced cohorts, significantly enhancing the reliability of the conclusion. This aligns with prior research: the

Table 2 Evaluation of treatment response and comparison between groups in a single-center cohort

Variables	Total (n=44)	RT (n=16)	Stupp (n=15)	RT→TMZ (n=13)	P
Treatment response, n (%)					0.937
PD	10 (22.7%)	4 (25.0%)	3 (20.0%)	3 (23.1%)	
PR	12 (27.3%)	3 (18.8%)	5 (33.3%)	4 (30.8%)	
SD	22 (50.0%)	9 (56.2%)	7 (46.7%)	6 (46.1%)	
DCR, n (%)					1.000
No	10 (22.7%)	4 (25.0%)	3 (20.0%)	3 (23.1%)	
Yes	34 (77.3%)	12 (75.0%)	12 (80.0%)	10 (76.9%)	
ORR, n (%)					0.693
No	32 (72.7%)	13 (81.2%)	10 (66.7%)	9 (69.2%)	
Yes	12 (27.3%)	3 (18.8%)	5 (33.3%)	4 (30.8%)	

Note: SD: Stable Disease; PR: Partial Response; DCR: Disease Control Rate; ORR: Objective Response Rate

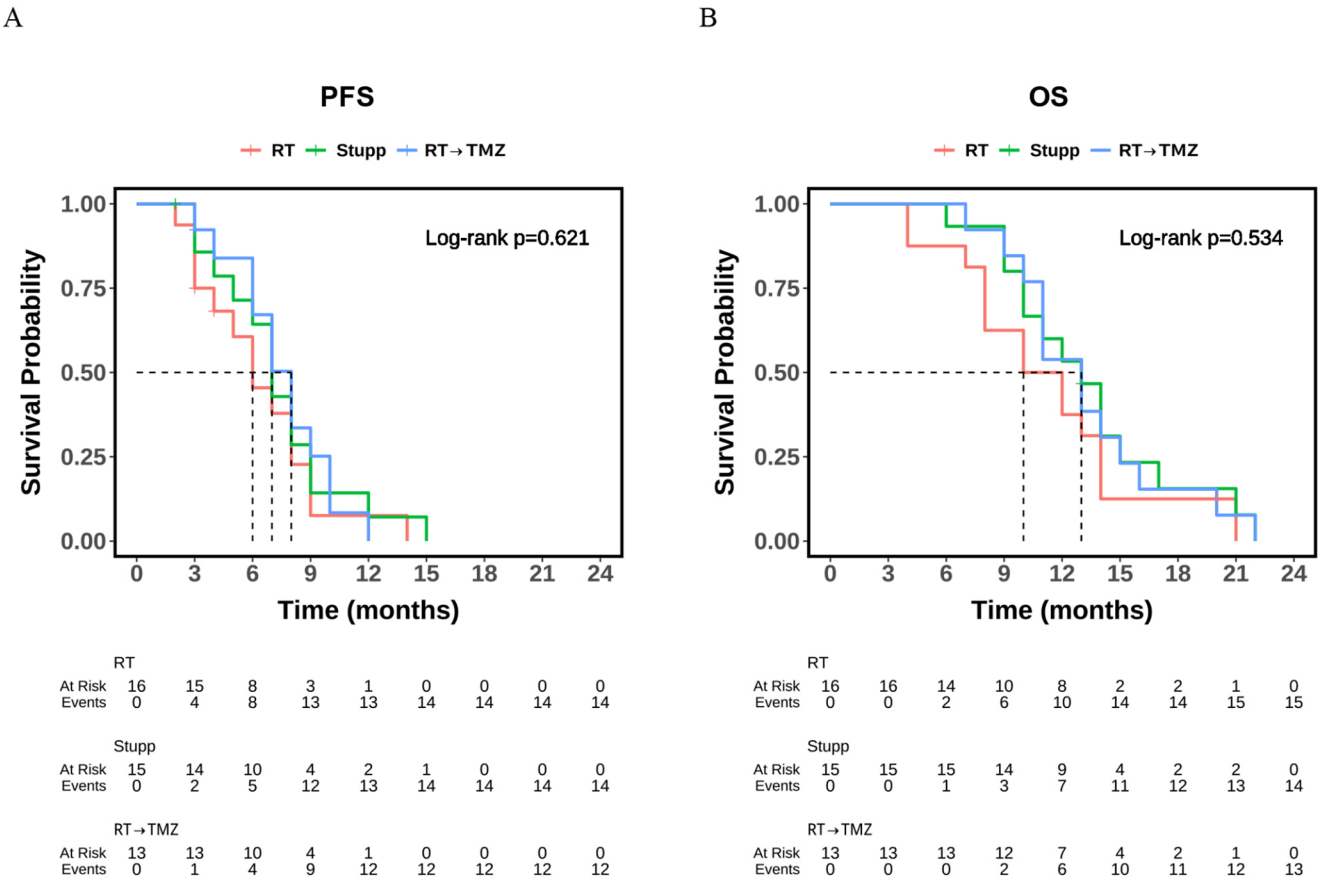

Fig. 1 PFS and OS survival curves of different treatment regimens in the single-center cohort, RT: Radiotherapy alone group; Stupp: Radiotherapy combined with concurrent and adjuvant temozolomide chemotherapy group; RT→TMZ: Radiotherapy followed by temozolomide chemotherapy group

ACNS0927 trial and several meta-analyses have shown no survival benefit from conventional cytotoxic chemotherapy in DIPG [15, 28, 29]. Our study provides the first systematic validation of this finding specifically within a Chinese cohort of H3K27M-mutant DIPG, further consolidating the international consensus that traditional chemotherapy is ineffective for this molecular subtype.

The lack of efficacy likely stems from the unique biological characteristics of DIPG: (1) The blood-brain barrier limits TMZ delivery, with DCE-MRI suggesting lower vascular permeability compared to adult glioblastoma [30, 31]; (2) The MGMT promoter methylation rate is low (approximately 20–30%) and its predictive value remains unclear [32, 33]; (3) The H3K27M mutation induces global

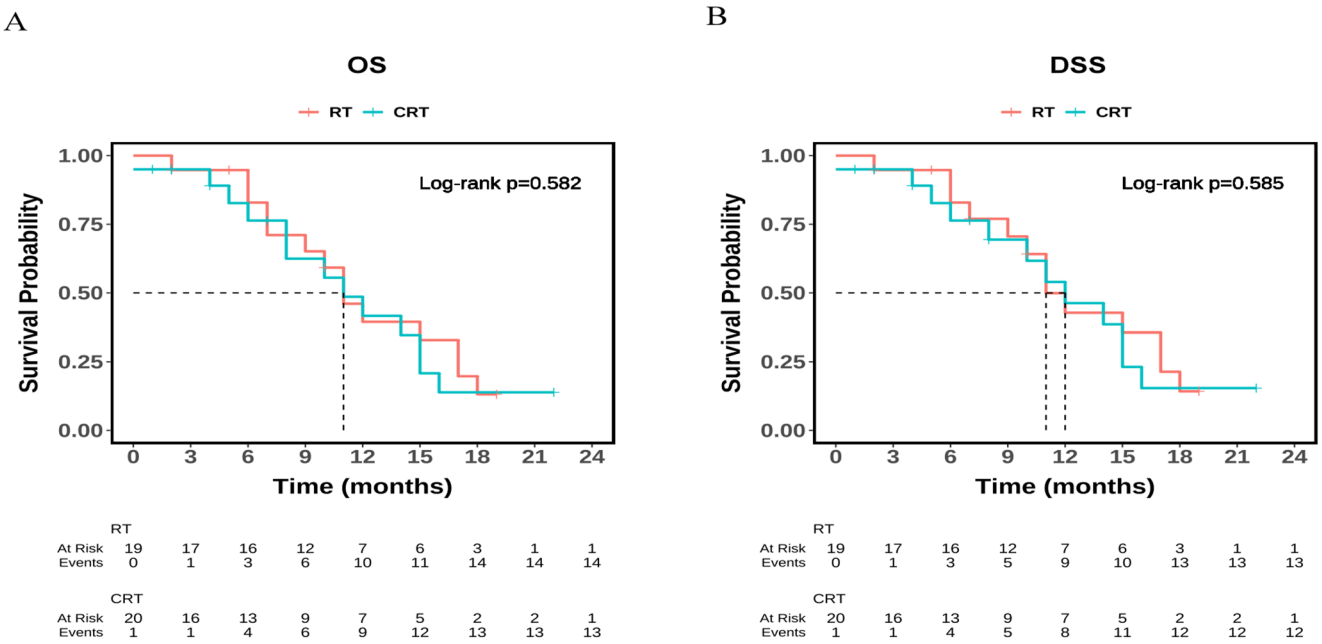

Fig. 2 OS and DSS survival curves of different treatment regimens in the SEER Cohort, RT: radiotherapy alone, CRT: chemoradiotherapy (radiotherapy plus chemotherapy)

epigenetic dysregulation, upregulating DNA repair and anti-apoptotic signaling pathways [34, 35]; (4) An immunosuppressive microenvironment and the presence of cancer stem cell subpopulations mediate intrinsic resistance [36–38]. These factors collectively contribute to the innate resistance of H3K27M-mutant DIPG to alkylating agents.

Regarding safety, the Stupp regimen (concurrent+adjuvant TMZ) was associated with significantly increased risks of leukopenia and liver function injury, along with a trend towards more grade ≥ 3 AEs, consistent with reports by Broniscer et al. [17]. In contrast, sequential TMZ administered after RT did not result in significantly increased toxicity, suggesting better tolerability. Given the absence of a survival benefit with concurrent chemoradiotherapy and its clear toxicity profile, clinical decision-making should weigh risks and benefits: for children with poor performance status or where quality of life is the priority, RT alone, or sequentially administered TMZ after informed consent, may represent a more reasonable individualized choice.

In this study, bevacizumab was used only as salvage therapy after radiographic or clinical progression, not as first-line treatment. Its primary role was to control severe peritumoral edema and alleviate symptoms of increased intracranial pressure, rather than to exert direct antineoplastic effects. Although temporary symptomatic improvement was observed, no objective tumor response or survival benefit was achieved. Therefore, the use of bevacizumab in H3K27M-mutant DIPG should be limited to palliative anti-edema management and should not be promoted as a routine antineoplastic strategy.

This study has limitations inherent to its retrospective, non-randomized design, including selection bias and potential confounding factors. The sample size of the single-center cohort was limited, which might have underpowered the detection of a modest benefit from TMZ in specific subgroups. The SEER database lacks detailed information on specific chemotherapy regimens (drugs, doses, cycles), introducing heterogeneity within the CRT group. Furthermore, patient-reported outcomes were not assessed. Future efforts should focus on establishing prospective multicenter cohorts, systematically exploring the predictive value of biomarkers such as MGMT, and concentrating on innovative strategies including epigenetic modifiers, immunotherapies, and novel drug delivery systems. Concurrently, developing prognostic models integrating clinical and molecular features, along with comprehensive quality of life assessments, will be crucial for optimizing clinical practice. Additionally, this retrospective study did not systematically screen for pseudoprogression using predefined imaging criteria (e.g., MRS, PWI, or short-interval follow-up MRI). While no unequivocal case of pseudoprogression was identified in our cohort, the possibility of misclassification of individual cases as true progression cannot be entirely excluded. Given that OS is a hard endpoint unaffected by such misclassification and that the between-group comparison of PFS is unlikely to be systematically biased, the impact of this limitation on our primary conclusions is limited. Future prospective studies should adopt standardized imaging assessment protocols to clarify the true incidence of pseudoprogression and its implications for treatment evaluation.

Table 3 Comparison of AEs rates between the RT and stupp groups and between the RT and RT→TMZ groups in the single-center cohort

Characteristic	Group		P	Group		P
	RT (N = 16)	Stupp (N = 15)		RT (N = 16)	RT→TMZ (N = 13)	
Leukopenia, n (%)			0.015			0.064
No	15 (93.8%)	8 (53.3%)		15 (93.8%)	8 (61.5%)	
Yes	1 (6.2%)	7 (46.7%)		1 (6.2%)	5 (38.5%)	
Neutropenia, n (%)			0.22			0.364
No	14 (87.5%)	10 (66.7%)		14 (87.5%)	9 (69.2%)	
Yes	2 (12.5%)	5 (33.3%)		2 (12.5%)	4 (30.8%)	
Thrombocytopenia, n (%)			0.333			0.299
No	15 (93.8%)	12 (80.0%)		15 (93.8%)	10 (76.9%)	
Yes	1 (6.2%)	3 (20.0%)		1 (6.2%)	3 (23.1%)	
Lymphopenia, n (%)			0.083			0.144
No	15 (93.8%)	10 (66.7%)		15 (93.8%)	9 (69.2%)	
Yes	1 (6.2%)	5 (33.3%)		1 (6.2%)	4 (30.8%)	
Elevated ALT, n (%)			0.002			0.144
No	15 (93.8%)	6 (40.0%)		15 (93.8%)	9 (69.2%)	
Yes	1 (6.2%)	9 (60.0%)		1 (6.2%)	4 (30.8%)	
Elevated AST, n (%)			0.006			0.064
No	15 (93.7%)	7 (46.7%)		15 (93.8%)	8 (61.5%)	
Yes	1 (6.3%)	8 (53.3%)		1 (6.2%)	5 (38.5%)	
Dizziness, n (%)			0.156			0.274
No	11 (68.8%)	6 (40.0%)		11 (68.8%)	6 (46.2%)	
Yes	5 (31.2%)	9 (60.0%)		5 (31.2%)	7 (53.8%)	
Headache, n (%)			0.289			
No	10 (62.5%)	6 (40.0%)		10 (62.5%)	7 (53.9%)	0.716
Yes	6 (37.5%)	9 (60.0%)		6 (37.5%)	6 (46.1%)	
Epilepsy, n (%)			0.252			0.667
No	13 (81.2%)	9 (60.0%)		13 (81.2%)	9 (69.2%)	
Yes	3 (18.8%)	6 (40.0%)		3 (18.8%)	4 (30.8%)	
Nausea and vomiting, n (%)			0.22			0.238
No	6 (37.5%)	2 (13.3%)		6 (37.5%)	2 (15.4%)	
Yes	10 (62.5%)	13 (86.7%)		10 (62.5%)	11 (84.6%)	
AEs of WHO Grade ≥3, n (%)			0.113			0.364
No	14 (87.5%)	9 (60.0%)		14 (87.5%)	9 (69.2%)	
Yes	2 (12.5%)	6 (40.0%)		2 (12.5%)	4 (30.8%)	

RT: Radiotherapy alone group; Stupp: Radiotherapy combined with concurrent and adjuvant temozolomide chemotherapy group. RT→TMZ: Radiotherapy followed by temozolomide group

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (project number: TA2022-145 and ethics approval number: L/G2022-K001-003). This study was performed according to the principles of the Declaration of Helsinki.

Consent to participate Written informed consent was obtained from the parents or legal guardians of all pediatric patients (<18 years of age) prior to study enrollment. For patients aged 7 years or older, verbal assent was also obtained from the child. For telephone follow ups, verbal informed consent was obtained from the guardians before each contact.

Consent to publish The authors affirm that human research participants provided informed consent for publication.

Competing interests The authors declare no competing interests.

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