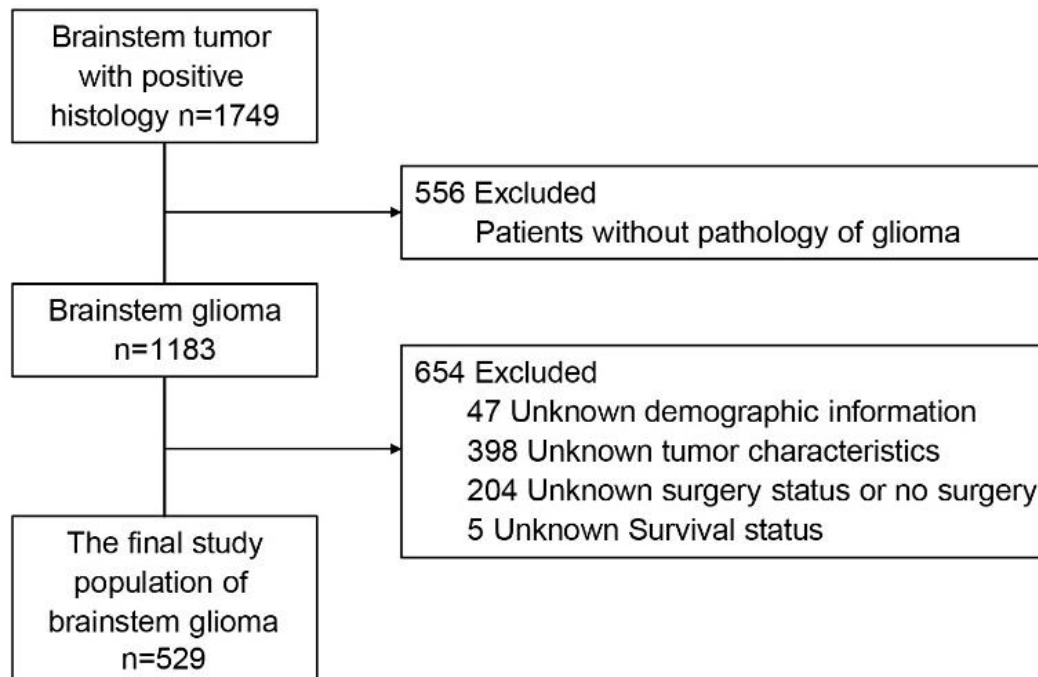
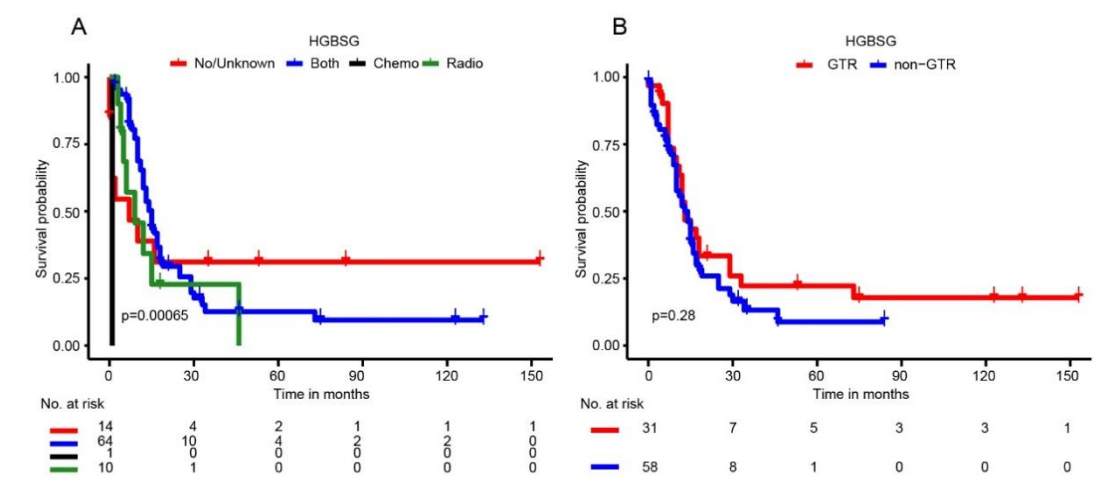


Supplement Figure 1 Flowchart of patient with histologically confirmed brainstem glioma selection



Supplement Figure2 Kaplan-Meier curves by (A) adjuvant therapy (B) GTP and non-GTP in HGBSG patient group.



Supplement Table 1 The distribution of extent of surgery and adjuvant therapy in 4 different patient groups

	Pediatric LGBSG N (%)	Pediatric HGBSG N (%)	Adult LGBSG N (%)	Adult HGBSG N (%)	P-value
Population size	236 (100)	37 (100)	204 (100)	52 (100)	
5-year CSS rates	88.6%	18.6%	82.1%	11.3%	
Extent of surgery					<0.001 [†]
Biopsy	47 (19.9)	11 (29.7)	48 (23.5)	21 (40.4)	
STR	44 (18.6)	12 (32.4)	39 (19.1)	14 (26.9)	
GTR	145 (61.4)	14 (37.8)	117 (57.4)	17 (32.7)	
Adjuvant Therapy					<0.001 [†]
No/Unknown	110 (46.6)	4 (10.8)	101 (49.5)	10 (19.2)	
Radiotherapy	53 (22.5)	4 (10.8)	73 (35.8)	6 (11.5)	
Chemotherapy	46 (19.5)	0 (0.0)	2 (1.0)	1 (1.9)	
Both	27 (11.4)	29 (78.4)	14 (6.9)	35 (67.3)	

Note: [†]P<0.05, statistically significant.

Supplement table 2 The result of univariate and multivariate analysis of extent of resection and adjuvant therapy in HGBSG patient groups

Treatment options	Univariate analysis		Multivariable analysis	
	HR(95%CI)	P-value	HR(95%CI)	P-value
Surgery				
Biopsy	1 [Reference]		1 [Reference]	
STR	0.57 (0.31-1.03)	0.064	0.67 (0.33-1.37)	0.33
GTR	0.59 (0.33-1.02)	0.059	0.74 (0.40-1.57)	0.27
Adjuvant therapy				
None/unknown	1 [Reference]		1 [Reference]	
Radiotherapy	1.54 (0.58-4.02)	0.38	1.29 (0.47-3.55)	0.621
Chemotherapy	22.04(2.37-205.17)	0.006 [†]	10.74(1.03-111.87)	0.047 [†]
Both	1.02 (0.50-2.10)	0.95	0.61(0.25-1.46)	0.27

Supplement Table 3 The distribution of histologic type in pediatric and adult patient groups

	GTR rate	ALL N (%)	Pediatric N (%)	Adult N (%)
Population size	55.3%	529(100)	273(100)	256(100)
Pilocytic astrocytoma (I)	58.0%	200(37.8)	144(52.7)	56(21.9)
Astrocytoma, NOS (II)	36.0%	50(9.5)	26(9.5)	24 (9.4)
Diffuse astrocytoma (II)	5/10	10(1.9)	5(1.8)	5(2.0)
Ependymoma/anaplastic ependymoma(II)	68.2%	176(33.3)	60(22.0)	116(45.3)
Oligodendroglioma(II)	1/1	1(0.2)	1(0.4)	0(0.0)
Unique astrocytoma variants(II)	2/3	3(0.6)	0(0.0)	3(1.2)
Anaplastic astrocytoma(III)	29.6%	27(5.1)	11(4.0)	16(6.3)
Anaplastic oligodendroglioma(III)	1/1	1(0.2)	0(0.0)	1(0.4)
Mixed glioma(III)	2/5	5(0.9)	2(0.7)	3(1.2)
Neuroepithelial (III)	1/1	1(0.2)	1(0.4)	0(0.0)
Glioblastoma (IV)	36.4%	55(10.4)	23(8.4)	32(12.5)

Supplement Table 4 Patient demographics, tumor characteristics and treatment options between different histology types in LGBSG group

Characteristics	EP N (%)	PA N (%)	OLG N (%)	P-Value
Population Size	176 (100)	200 (100)	61 (100)	
Age group				<0.001 [†]
Pediatric	60 (34.1)	144(72.0)	32 (52.5)	
Adult	116 (65.9)	56 (28.0)	29 (47.5)	
Sex				0.12
Female	73(41.5)	104 (52.0)	30 (49.2)	
Male	103(58.5)	96 (48.0)	31 (50.8)	
Race				0.12
Other	10 (5.7)	16 (8.0)	0 (0.0)	
Black	17 (9.7)	14 (0.7)	8 (13.1)	
White	149 (84.7)	170(85.0)	53 (86.9)	
Marital status				<0.001 [†]
Unmarried	96 (54.5)	170 (85.0)	42 (68.9)	
Married	80 (45.5)	30 (15.0)	19 (31.1)	
Size				0.36
<4.8cm	128(72.7)	157 (78.5)	44 (72.1)	
≥4.8cm	48 (27.3)	43 (21.5)	17 (27.9)	
Extension				<0.001 [†]
Brainstem	44 (25.0)	92 (46.0)	35 (57.4)	
Cerebellum	20 (11.4)	18 (9.0)	6 (9.8)	
Ventricular	81 (46.0)	58(29.0)	8(13.1)	
Other	31 (17.6)	32 (16.0)	12 (19.7)	
Metastasis				0.91
No	172 (97.7)	195 (97.5)	59 (96.7)	
Yes	4 (2.3)	5 (2.5)	2 (3.3)	
Adjuvant therapy				<0.001 [†]
None/unknown	59 (33.5)	144 (72.0)	18 (29.5)	
Both	14 (8.0)	8 (4.0)	18 (29.5)	
Radiotherapy	94 (53.4)	14 (7.0)	20 (32.8)	
Chemotherapy	9 (5.1)	34 (17.0)	5 (8.2)	
Surgical resection				<0.001 [†]
Biopsy	31(17.6)	41(20.5)	22(36.1)	
STR	25(14.2)	43(21.5)	15(24.6)	
GTR	120(68.2)	116(58.0)	24(39.3)	
Vital status				<0.001 [†]
Alive	143 (81.3)	185 (92.5)	33 (54.1)	
Dead	33 (18.8)	15 (7.5)	32 (52.5)	
Cancer specific vitals				<0.001 [†]
Alive	155 (88.1)	187 (93.5)	33 (54.1)	
Dead	21 (11.9)	13 (6.5)	28 (45.9)	

Note: [†]P<0.05, statistically significant.

Supplement Table 5 Review of clinical studies of brainstem glioma with histological diagnosis

Study	Patient group	N ^a	Surgery related Mortality /Morbidity	GTR rate	Surgical resection
Sinha S ²⁶	Well delineated BSG	58	5%/19%	/	90% patients improved neurological status after surgery
Wang CC ¹⁴	BSG	311	1.3%/27.6 %	40.5%	LGBSG had higher GTR rate and better survival outcome after surgery
Teo C ¹⁹	Focal BSG	34	0/18.8%	35.2%	LGBSG had higher GTR rate
Lesniak MS ³²	Contrast-enhanced Pediatric BSG	57	0/22.7%	50.8%	Juvenile pilocytic astrocytoma had the best survival outcome after surgery.
Mottolese C ²⁰	Tectal plate Pediatric BSG	27	0/18.5%	60%	Exophytic Tectal plate glioma could be treated with surgical resection safely.
Sun T ²⁴	Pediatric BSG	33	/	21.2%	LGBSG has better survival outcome after surgery.
Holzapfel J ¹⁵	Pediatric LGBSG	116	0/21%	10%	GTR significantly related to better PFS but not OS.
Upadhyay a SA ¹⁶	Pediatric LGBSG	23	0/21.7%	17.4%	GTR was related to better survival outcome but not significantly.
Sandri A ²⁹	Focal Pediatric LGBSG	17	0/17.6%	13.5%	GTR was significantly related to better PFS but not OS.
Ahmed KA ¹⁷	Pediatric LGBSG	48	/	8.3%	Surgical resection significantly improved survival outcome
Klimo P Jr ²⁸	Pediatric LGBSG	52	9.6%/36.5%	17%	GTR was significantly related to better PFS but not OS.
Tasic G ³¹	Adult BSG	48	/	3.9%	LGBSG had better survival outcome after surgery.
Reithmeier T ²²	Adult BSG	104	0/11.6%	2%	GTR was not significantly related to survival outcome
Kesari S ²¹	Adult BSG	28	0/29%	/	GTR was not significantly related with survival outcome
Majchrzak K ¹³	Adult BSG	47	4.2%/45%	30%	Focal tectal and exophytic BSG and had higher GTR rate and better prognosis

Note: N^a, number of patients with histological diagnosis in the study cohort.

