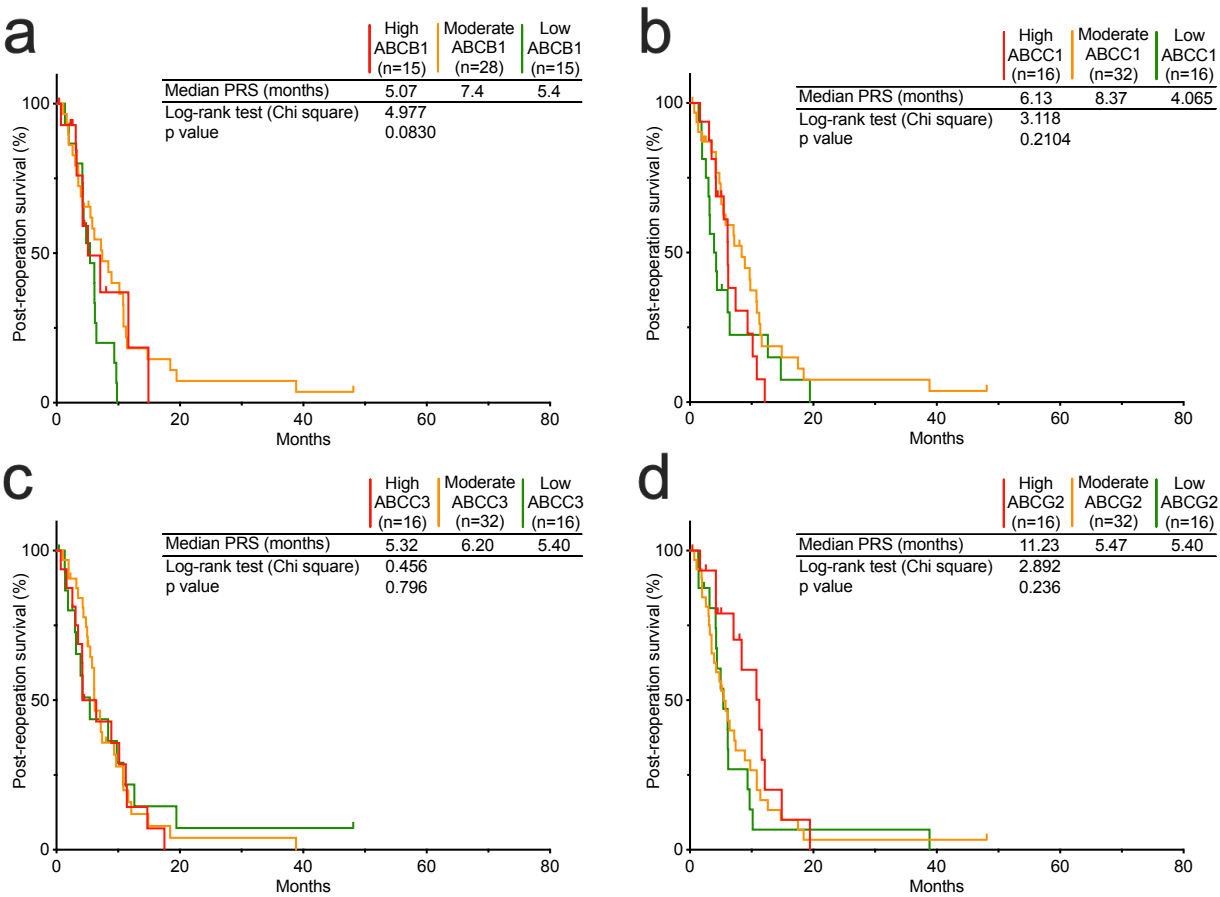
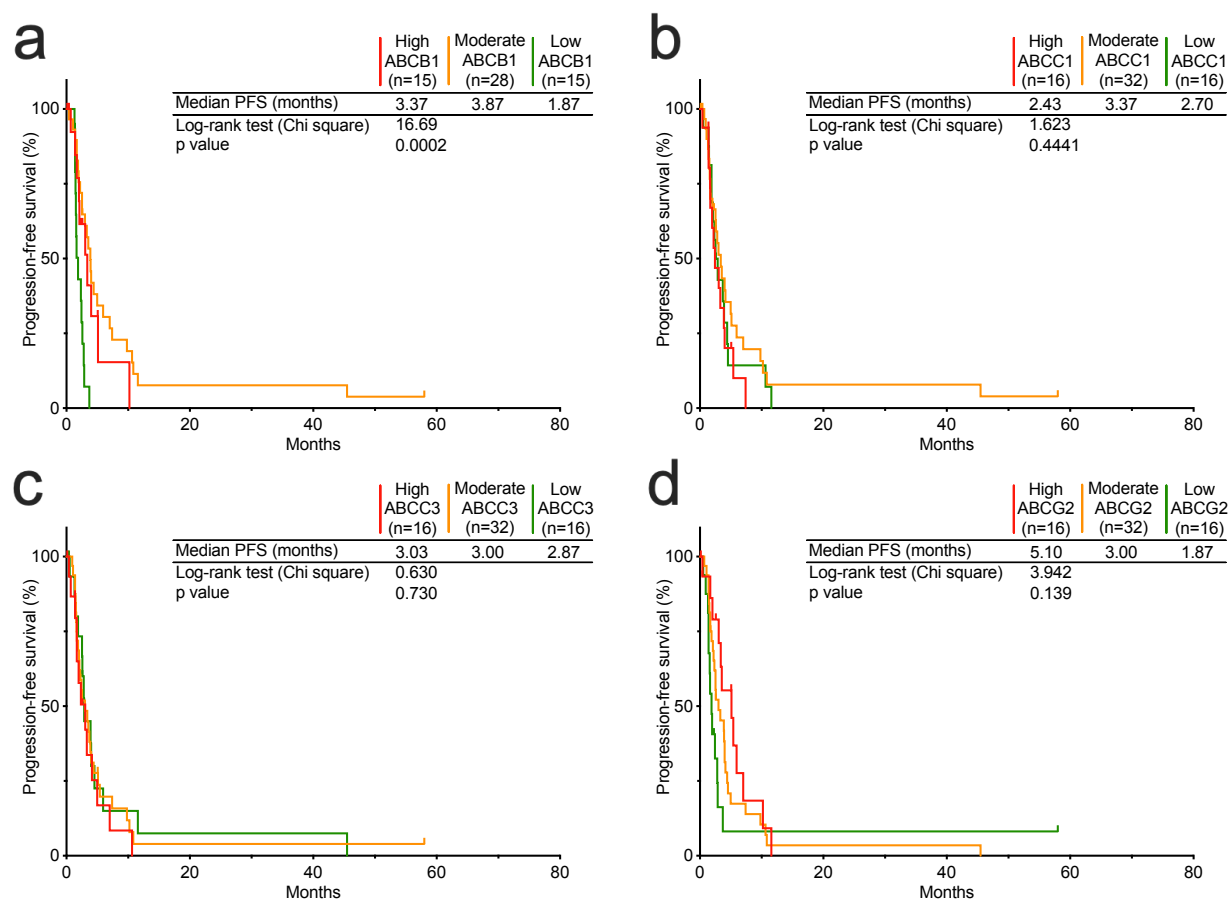


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Supplementary figure 1 Correlation of ABC transporters expression level with recurrent GBM patient outcome. Kaplan–Meier estimates of post-reoperation survival in newly diagnosed GBM according to ABCB1 (a), ABCC1 (b), ABCC3 (c) and ABCG2 (d)

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Supplementary figure 2 Correlation of ABC transporters expression level with recurrent GBM patient outcome. Kaplan–Meier estimates of progression-free survival in newly diagnosed GBM according to ABCB1 (a), ABCC1 (b), ABCC3 (c) and ABCG2 (d)

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Supplementary table 1 List of genes and sequences of primers & probes used in the qPCR experiments

Gene	Forward	Reverse	Probe
ATP Binding Cassette Subfamily B Member 1 (ABCB1)	5'-CTTCAGGGTTTCACATTTGGC-3'	5'-GGTAGTCAATGCTCCAGTGG-3'	5'-/56-FAM/TGGTTTTCCGATCCATGCTCAGACAG/3IABkFQ/-3'
ATP Binding Cassette Subfamily C Member 1 (ABCC1)	5'-GACCCTCCCACTGAATG-3'	5'-CCTCCACTTTGTCCATCTCAG-3'	5'-/56-FAM/CGACTTTC CGCAGCCCACCT/3IABkFQ/-3'
ATP Binding Cassette Subfamily C Member 3 (ABCC3)	5'-ACCTGTCCAAGCTCAAGATG -3'	5'-GGGTGACAAAGAAAACAGGG-3'	5'-/56-FAM/AAAAGGTCC GCCCAGGAGACG/3IABkFQ/-3'
ATP Binding Cassette Subfamily G Member 2 (ABCG2)	5'-CGATATGGATTACGGCTTTGC-3'	5'-AGATCGATGCCCTGCTTTAC-3'	5'-/56-FAM/CCCAGGACTCAATG CAACAGGAAACA/3IABkFQ/-3'
Hypoxanthine Phosphoribosyltransferase (HPRT)	5'-GACTTTGCTTTCTTGGTCAG-3'	5'-GGCTTATATCCAACACTTCGTG-3'	5'-/56-FAM/ATGGTCAAGGTGCGC AAGCTTGCTGGT/3IABkFQ/-3'
Serine and Arginine Rich Splicing Factor 9 (SFRS9)	5'-TGTGCAGAAGGATGGAGT-3'	5'-CTGGTGCTTCTCTCAGGATA-3'	5'-/5MAXN/TGGAATATGCCCT GCGTAAACTGGA/3IABkFQ/-3'
TATA-box Binding Protein (TBP)	5'-CACGAACCACGGCACTGATT -3'	5'-TTTTCTTGCTGCCAGTCTGGAC-3'	5'-/56-FAM/TGTGCACAGGAGC CAAGAGTGAAGA/3IABkFQ/-3'

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	Newly diagnosed	Recurrent
N	95	64
Age at diagnosis (years)		
Median	62	53
Range	23-83	26-75
Age classes, n (%)		
50 years or younger	21 (22.1)	27 (42.2)
51-60 years	24 (25.3)	19 (29.7)
61-70 years	26 (27.4)	14 (21.9)
70 years or older	24 (25.3)	4 (6.3)
Sex, n (%)		
Female	44 (46.3)	27 (42.2)
Male	51 (53.7)	37 (57.8)
KPS (pre-operative), n (%)		
90-100	20 (21.1)	9 (14.1)
70-80	27 (28.4)	21 (32.8)
50-60	31 (32.6)	14 (21.9)
50 or lower	17 (17.9)	20 (31.3)
Tumor location at diagnosis, n (%)		
Frontal	43 (45.3)	22 (34.4)
Temporal	15 (15.8)	13 (20.3)
Parietal	16 (16.8)	6 (9.4)
Occipital	0 (0)	1 (1.6)
Not circumscribed to one lobe	21 (22.1)	22 (34.4)
Right hemisphere	56 (58.9)	27 (42.2)
Left hemisphere	37 (38.9)	37 (57.8)
Not circumscribed to one hemisphere	2 (2.1)	0 (0)
Deep seeded	4 (4.2)	2 (3.1)
Extent of resection, n (%)		
Gross total	51 (53.7)	16 (25)
Partial	39 (41.1)	43 (67.2)
Biopsy	5 (5.3)	5 (7.8)
Histological subtype, n (%)		
Glioblastoma	69 (72.6)	55 (85.9)
Glioblastoma with oligodendroglial component	22 (23.2)	8 (12.5)
Glioblastoma with PNET component	1 (1.1)	0 (0)
Glioblastoma with gemistocytic component	2 (2.1)	0 (0)
Glioblastoma with small cell component	1 (1.1)	0 (0)
Gliosarcoma	0 (0)	1 (1.6)
First line therapy, n (%)		
Stupp	71 (74.7)	52 (81.3)
RT alone	4 (4.2)	5 (7.8)
RTsc alone	12 (12.6)	2 (3.1)
TMZ alone	2 (2.1)	0 (0)
No treatment	6 (6.3)	2 (3.1)
Second line therapy, n (%)		
TTF	1 (1.1)	0 (0)
TMZ alone	34 (35.8)	22 (34.4)
GK	0 (0)	3 (4.7)
IAC	13 (13.7)	33 (51.6)
CCNU	4 (4.2)	2 (3.1)
Avastin	4 (4.2)	0 (0)
No treatment	37 (38.9)	4 (6.3)
N/A	2 (2.1)	0 (0)
Received third line therapy or more	22 (23.2)	26 (34.4)
Survival (months)		
Median OS (95% CI; events)	13.5 (11.1-16.8; 78)	24.0 (16.8-26.6; 56)
Received first line Stupp	16.9 (13.7-22.4; 56)	24.5 (13.7-22.4; 47)
Did not receive first line Stupp	5.3 (2.8-10.97; 22)	11.4 (2.8-56.3; 9)
Median PRS (95% CI; events)	N/A	5.5 (4.4-7.2; 56)
Median PFS (95% CI; events)	5.1 (3.9-7.4; 87)	3.0 (2.3-4.0; 55)
Received first line Stupp	6.6 (4.6-11.4; 67)	N/A
Did not receive first line Stupp	2.7 (1.3-4.5; 20)	N/A
Alive at last followup, n (%)	17 (17.9)	8 (12.5)

Supplementary Table 2 Patients characteristics. PNET, primitive neuroectodermal tumour; RT, radiotherapy; RTsc, short course radiotherapy, TMZ, temozolomide; TTF, tumour treating fields; GK, gamma-knife; IAC, intra-arterial chemotherapy; N/A, not applicable; OS, overall survival; PRS, post-reoperation survival; PFS, progression-free survival

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Supplementary table 3 Univariate and multivariate analyses for overall survival in newly diagnosed GBMs. Only the variables with a significant p value for the univariate analysis were included in the multivariate analysis. KPS, Karnofsky Performance Status; NRQ, normalized relative quantity; Celldex, Rindopepimut - injectable peptide vaccine targeting epidermal growth factor receptor variant III (EGFRvIII); TTF, tumour treating fields; Metmab, onartuzumab - monoclonal antibody against hepatocyte growth factor receptor (c-Met)

Variables	Univariate			Multivariate		
	Hazard Ratio	C.I. 95%	p value	Hazard Ratio	C.I. 95%	p value
Gender (M vs F)	1.188	0.759 - 1.859	0.452			
Age	1.037	1.018 - 1.055	<0.000	1.023	1.003 - 1.043	0.023
KPS (preoperative)	0.985	0.971 - 0.999	0.034	0.998	0.981 - 1.015	0.776
mRNA expression data						
NRQ ABCB1	0.882	0.601 - 1.294	0.521			
NRQ ABCC1	1.175	0.954 - 1.447	0.128			
NRQ ABCC3	1.026	0.962 - 1.093	0.438			
NRQ ABCG2	0.826	0.693 - 0.984	0.032	0.905	0.771 - 1.063	0.223
Tumor location						
Frontal (yes vs no)	0.684	0.437 - 1.071	0.097			
Temporal (yes vs no)	0.862	0.531 - 1.399	0.548			
Parietal (yes vs no)	1.526	0.941 - 2.473	0.086			
Occipital (yes vs no)	2.531	1.076 - 5.951	0.033	2.289	0.916 - 5.719	0.076
Right hemisphere (yes vs no)	1.044	0.662 - 1.644	1.044			
Left hemisphere (yes vs no)	0.851	0.534 - 1.354	0.495			
Deep seeded (yes vs no)	2.126	0.772 - 5.855	0.144			
Extent of resection						
Gross total (yes vs no)	0.884	0.566 - 1.381	0.589			
Partial (yes vs no)	1.036	0.659 - 1.628	0.878			
Biopsy (yes vs no)	1.569	0.626 - 3.933	0.337			
Treatment modality						
Stupp (yes vs no)	0.189	0.108 - 0.332	<0.000	0.408	0.053 - 3.164	0.391
Celldex (yes vs no)	0.877	0.402 - 1.914	0.742			
TTF (yes vs no)	0.934	0.129 - 6.750	0.946			
Radiotherapy (yes vs no)	3.666	1.296 - 10.367	0.014	1.366	0.141 - 13.239	0.788
Short course radiotherapy (yes vs no)	3.680	1.859 - 7.284	<0.000	1.341	0.171 - 10.494	0.780
Temozolomide alone (yes vs no)	2.110	0.286 - 15.563	0.464			
Intra-arterial chemotherapy (number of cycles)	0.939	0.856 - 1.030	0.182			
Metmab (yes vs no)	0.947	0.344 - 2.607	0.916			
CCNU (yes vs no)	2.296	0.702 - 7.512	0.169			
Avastin (yes vs no)	2.410	0.864 - 6.720	0.093			
Combined (yes vs no)	0.979	0.624 - 1.537	0.927			
No treatment (yes vs no)	4.877	2.077 - 11.452	<0.000	1.751	0.198 - 15.495	0.615

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Supplementary table 4 Univariate and multivariate analyses for progression-free survival in newly diagnosed GBMs. Only the variables with a significant p value for the univariate analysis were included in the multivariate analysis. KPS, Karnofsky Performance Status; NRQ, normalized relative quantity; Celldex, Rindopepimut - injectable peptide vaccine targeting epidermal growth factor receptor variant III (EGFRvIII); TTF, tumour treating fields; Metmab, onartuzumab - monoclonal antibody against hepatocyte growth factor receptor (c-Met)

Variables	Univariate			Multivariate		
	Hazard Ratio	C.I. 95%	p value	Hazard Ratio	C.I. 95%	p value
Gender (M vs F)	1.401	0.908 - 2.161	0.128			
Age	1.026	1.009 - 1.043	0.002	1.017	0.997 - 1.037	0.100
KPS (preoperative)	0.996	0.982 - 1.010	0.589			
mRNA expression data						
NRQ ABCB1	0.859	0.569 - 1.296	0.469			
NRQ ABCC1	1.357	1.084 - 1.699	0.008	1.533	1.128 - 2.084	0.006
NRQ ABCC3	1.063	1.000 - 1.130	0.050	0.988	0.909 - 1.074	0.779
NRQ ABCG2	0.891	0.766 - 1.036	0.132			
Tumor location						
Frontal (yes vs no)	0.669	0.437 - 1.024	0.064			
Temporal (yes vs no)	0.799	0.505 - 1.262	0.336			
Parietal (yes vs no)	1.794	1.136 - 2.832	0.012	1.572	0.934 - 2.644	0.088
Occipital (yes vs no)	1.851	0.846 - 4.049	0.123			
Right hemisphere (yes vs no)	0.909	0.591 - 1.401	0.667			
Left hemisphere (yes vs no)	0.976	0.636 - 1.498	0.911			
Deep seeded (yes vs no)	3.596	1.284 - 10.076	0.015	6.382	2.145 - 18.987	0.001
Extent of resection						
Gross total (yes vs no)	1.020	0.666 - 1.563	0.926			
Partial (yes vs no)	0.904	0.585 - 1.397	0.649			
Biopsy (yes vs no)	1.526	0.615 - 3.784	0.362			
Treatment modality						
Stupp (yes vs no)	0.305	0.177 - 0.525	<0.000	0.468	0.198 - 1.105	0.083
Celldex (yes vs no)	0.815	0.407 - 1.633	0.564			
TTF (yes vs no)	1.149	0.159 - 8.319	0.891			
Radiotherapy (yes vs no)	1.890	0.591 - 6.048	0.283			
Short course radiotherapy (yes vs no)	3.383	1.734 - 6.603	<0.000	1.619	0.567 - 4.623	0.368
Temozolomide alone (yes vs no)	4.340	1.015 - 18.554	0.048	2.243	0.434 - 11.597	0.335
Intra-arterial chemotherapy (number of cycles)	0.966	0.890 - 1.049	0.414			
Metmab (yes vs no)	0.794	0.290 - 2.175	0.654			
CCNU (yes vs no)	1.801	0.652 - 4.974	0.256			
Avastin (yes vs no)	3.959	1.380 - 11.360	0.011	8.461	2.738 - 26.148	<0.000
Combined (yes vs no)	1.136	0.736 - 1.753	0.566			
No treatment (yes vs no)	1.929	0.699 - 5.319	0.204			

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Supplementary table 5 Univariate and multivariate analyses for post-reoperation survival in recurrent GBMs. Only the variables with a significant p value for the univariate analysis were included in the multivariate analysis. KPS, Karnofsky Performance Status; NRQ, normalized relative quantity; Metmab, onartuzumab - monoclonal antibody against hepatocyte growth factor receptor (c-Met)

Variables	Univariate			Multivariate		
	Hazard Ratio	C.I. 95%	p value	Hazard Ratio	C.I. 95%	p value
Gender (M vs F)	0.988	0.577 - 1.691	0.965			
Age	1.019	0.997 - 1.040	0.084			
KPS (preoperative)	0.984	0.969 - 1.000	0.047	0.985	0.970 - 1.001	0.071
mRNA expression data						
NRQ ABCB1	0.930	0.739 - 1.171	0.537			
NRQ ABCC1	1.041	0.688 - 1.577	0.848			
NRQ ABCC3	1.005	0.873 - 1.156	0.949			
NRQ ABCG2	0.922	0.808 - 1.052	0.229			
Tumor location						
Frontal (yes vs no)	0.882	0.518 - 1.499	0.641			
Temporal (yes vs no)	1.081	0.635 - 1.839	0.774			
Parietal (yes vs no)	1.764	0.976 - 3.188	0.060			
Occipital (yes vs no)	1.185	0.501 - 2.804	0.699			
Right hemisphere (yes vs no)	0.912	0.529 - 1.572	0.740			
Left hemisphere (yes vs no)	1.096	0.636 - 1.890	0.740			
Deep seeded (yes vs no)	3.103	0.732 - 13.163	0.125			
Extent of resection						
Gross total (yes vs no)	0.547	0.279 - 1.074	0.080			
Partial (yes vs no)	1.361	0.753 - 2.460	0.308			
Biopsy (yes vs no)	2.052	0.802 - 5.246	0.134			
Treatment modality						
Stupp (yes vs no)	0.711	0.345 - 1.463	0.354			
Radiotherapy (yes vs no)	0.811	0.321 - 2.051	0.658			
Temozolomide alone (yes vs no)	0.617	0.350 - 1.087	0.094			
Gamma knife (yes vs no)	1.095	0.338 - 3.543	0.880			
Intra-arterial chemotherapy (number of cycles)	0.958	0.895 - 1.026	0.217			
CCNU (yes vs no)	1.142	0.154 - 8.455	0.896			
Combined (yes vs no)	1.022	0.367 - 2.849	0.967			
No treatment (yes vs no)	5.971	1.745 - 20.432	0.004	5.195	1.499 - 18.002	0.009

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Supplementary table 6 Univariate and multivariate analyses for progression-free survival in recurrent GBMs. Only the variables with a significant p value for the univariate analysis were included in the multivariate analysis. KPS, Karnofsky Performance Status; NRQ, normalized relative quantity; Metmab, onartuzumab - monoclonal antibody against hepatocyte growth factor receptor (c-Met)

Variables	Univariate			Multivariate		
	Hazard Ratio	C.I. 95%	p value	Hazard Ratio	C.I. 95%	p value
Gender (M vs F)	0.620	0.357 - 1.078	0.090			
Age	0.996	0.977 - 1.016	0.702			
KPS (preoperative)	0.996	0.980 - 1.011	0.586			
mRNA expression data						
NRQ ABCB1	0.862	0.645 - 1.153	0.317			
NRQ ABCC1	1.014	0.659 - 1.559	0.951			
NRQ ABCC3	1.047	0.897 - 1.222	0.560			
NRQ ABCG2	0.927	0.791 - 1.088	0.355			
Tumor location						
Frontal (yes vs no)	1.161	0.680 - 1.982	0.584			
Temporal (yes vs no)	0.929	0.543 - 1.589	0.787			
Parietal (yes vs no)	1.843	0.983 - 3.453	0.057			
Occipital (yes vs no)	1.115	0.440 - 2.827	0.819			
Right hemisphere (yes vs no)	1.102	0.643 - 1.890	0.724			
Left hemisphere (yes vs no)	0.907	0.529 - 1.556	0.724			
Deep seeded (yes vs no)	1.138	0.154 - 8.397	0.899			
Extent of resection						
Gross total (yes vs no)	0.603	0.603 - 0.603	0.603			
Partial (yes vs no)	1.248	1.248 - 1.248	1.248			
Biopsy (yes vs no)	3.699	3.699 - 3.699	3.699			
Treatment modality						
Stupp (yes vs no)	0.844	0.411 - 1.735	0.644			
Radiotherapy (yes vs no)	0.726	0.287 - 1.833	0.498			
Temozolomide alone (yes vs no)	0.902	0.520 - 1.566	0.715			
Gamma knife (yes vs no)	1.290	0.399 - 4.172	0.671			
Intra-arterial chemotherapy (number of cycles)	0.958	0.891 - 1.030	0.250			
CCNU (yes vs no)	0.047	0.000 - 128.396	0.449			
Combined (yes vs no)	0.681	0.241 - 1.926	0.469			
No treatment (yes vs no)	2.051	0.485 - 8.675	0.329			