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A Modern Radiotherapy Series of Survival in Hispanic Glioblastoma Patients

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Abstract

Background—Studies have shown racial differences in cancer outcomes. We investigate whether survival differences existed in Hispanic Glioblastoma (GBM) patients compared to other ethnicities from our modern radiotherapy series, as no study to date has focused on outcomes in this group after radiation therapy (RT).

Methods—We retrospectively evaluated 428 patients diagnosed with GBM from 1996–2014 at our institution, divided into four groups based on self-report: white, black, Hispanic, and Asian/Indian. The primary outcome was overall survival (OS). We analyzed differences in prognostic factors among the whole cohort compared to the Hispanic cohort alone.

Results—Baseline characteristics of the four racial groups were comparable. With a median follow-up of 387 days, no survival differences were seen by Kaplan-Meier analysis. Median OS for Hispanic patients was 355 days versus 450 days for the entire cohort. Factors significant for patient outcomes in the entire cohort differed slightly to those specific to Hispanic patients. Low

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Karnofsky Performance Status (KPS) was significant on multivariate analysis in the whole population, but not in Hispanic patients. Extent of resection, Recursive partitioning analysis (RPA) class, and RT total dose were significant on multivariate analysis in both the whole population and Hispanic patients.

Conclusions—We found Hispanic GBM patients had no difference in survival compared to other ethnicities in our cohort. Differences exist in factors associated with outcomes on single and multivariate analysis for Hispanic GBM patients compared to the entire cohort. Additional studies focusing on Hispanic patients will aid in more personalized treatment approaches in this group.

Keywords

Glioblastoma; Radiation Therapy; Hispanic; Ethnicity; Race

Introduction

Each year, glioblastoma (GBM) accounts for approximately 70% of new cases of malignant primary gliomas diagnosed in the United States.[1] The annual incidence of GBM is 3.19 cases per 100,000 in the United States alone, with 10,110 predicted cases in 2015.[2] Since the publication of the landmark study by Stupp and colleagues, the standard of treatment for GBM includes surgery followed by adjuvant chemoradiation with temozolomide.[3] Despite the multimodality treatment strategy, GBMs are associated with high morbidity and mortality, with a median survival ranging from 1.25 to 1.5 years.[1]

Ethnic and racial disparities in cancer outcome have been observed across many types of cancers, including GBM.[4–7] There are many possible contributors to these differences, including cultural and socioeconomic differences between ethnicities that can affect access to care and the type of treatment received, and thus contribute to differences in outcome.[8–10] Evidence also suggests that molecular variability occurs between ethnic groups.[11–13] Epidemiological and molecular studies have shown multiple factors correlated to differences in incidence rates of GBM as well as prognostic factors for outcome, including ethnicity, age at diagnosis, intracranial location, performance status, degree of resection and molecular/genetic variations.[14,15]

Hispanics have a much lower incidence of GBM in the United States, but represent the fastest-growing population in this country. The relative lack of studies focusing on outcomes in this population reveals a need for studies examining whether these patients have differences in prognostic factors and outcomes. Columbia Medical University Center (CUMC) is located in Washington Heights, New York, the population demographics of which include a 71.0% Hispanic population based on the US Census Bureau 2000 and 2010.[16] CUMC plays a large role in serving minority populations, and the Herbert Irving Comprehensive Cancer Center at CUMC is one of twelve recipients of the Minority/Underserved Community Site grants.[17] Our particular population distribution thus allows the opportunity to examine the outcomes of Hispanic GBM patients due to a higher volume of these patients being seen at our medical center.

Material and Methods

We reviewed all patients who underwent radiation therapy for GBM at Columbia University Medical Center from 1996 to 2014 from an Institutional Review Board-approved database. We collected baseline demographics as well as treatment related variables including: age at diagnosis, gender, marital status, Karnofsky Performance Status (KPS), extent of surgical resection, Recursive Partitioning Analysis (RPA) class, RT total dose, laterality, mulicentricity, isocitrate dehydrogenase 1 (IDH-1) status, O^6-methylguanine–DNA methyltransferase (MGMT) status, and temozolomide usage. The definition of race and ethnicity was based on patients' self-identification of their background. Extent of surgery was categorized as biopsy only, subtotal resection (STR), or gross total resection (GTR) by two study-blinded radiologists who reviewed the immediate pre- and post-operative MRI scans with comparison to pre-contrast T1 images. Residual tumor was defined as a single area of enhancement measuring 0.175 cm^3 or greater.[18] The primary outcome was overall survival (OS), determined as the time from surgery until death or last follow-up. Patients were stratified by ethnicity determined by patient-reported intake sheets: white, black, Hispanic, or Asian/Indian. Patients identifying as Hispanic were not included in the "white" and "black" populations, even if they self-identified in more than one group. We also analyzed differences in prognostic factors among the whole cohort and compared these to prognostic factors in the Hispanic cohort alone.

Statistical Methods

To compare baseline characteristics between the different ethnicities, contingency tables were generated using Pearson's chi-squared test for categorical variables and Fisher's Exact test when necessary. Actuarial survival curves were generated using the Kaplan-Meier survival model, and OS was compared by ethnicity using the Kaplan-Meier estimator and log-rank test. Univariate Cox regression analysis was performed among our cohort on variables expected to be significant predictors of mortality based on historical outcomes and existing literature. Variables found to be statistically significantly associated with survival on univariate analysis, as well as variables with expected clinical significance based on historical outcomes (even when p-values were bordering on significant) were considered for inclusion in the multivariate Cox regression model. Covariates in the final multivariate analysis were included in the model by step-wise selection. A p-value $< .05$ was considered significant for both univariate and multivariate analyses. The p-value was not adjusted for multiple comparisons. All analyses were performed using SPSS, version 22.

Results

A total of 428 patients were included in our analysis. Baseline demographics are in Table 1. Most patients were over the age of 50 (N=326, 76.2%) and 247 patients (57.7%) were men. There were 313 white (73.1%), 21 black (4.9%), 77 Hispanic (18.0%), and 17 Asian/Indian (4.0%) patients. Baseline characteristics were similar across all ethnicities with the notable exception of marital status: more white and Asian/Indian patients were married compared to black and Hispanic cohorts.

OS and survival stratified by ethnicity was assessed with Kaplan-Meier curves (Figure 1 and Table 2). Median follow up for the entire cohort was 387 days. There was no difference in OS between ethnic groups. The median OS for the entire cohort was 450 days with 95% confidence interval (CI) of 410–490 days. Median OS for white patients were 457 days (CI 414–500 days), black patients 449 days (CI 268–630 days), Hispanic patients 355 days (CI 275–435 days), and Asian/Indian patients 602 days (CI 495–709 days).

Univariate Cox regression analysis for the entire cohort showed no difference between ethnic groups. Increased hazard ratio for death (HR) was seen with age greater than or equal to 50 years of age (HR 1.826; CI 1.409–2.368); KPS less than 70 (HR 3.233; CI 2.452–4.262); extent of surgical resection: subtotal resection or biopsy versus gross total resection (HR 1.698; CI 1.182–2.440 and HR 2.992; CI 2.180–4.107, respectively); RPA class: IV and V/VI versus III (HR 2.357; CI 1.511–3.675 and HR 7.815; CI 4.816–12.681, respectively); RT total dose: less than 36 Gy and 36 to 54 Gy versus greater than 54 Gy (HR 4.526; CI 3.202–6.396 and HR 1.787; CI 1.158–2.757); and no temozolomide (TMZ) use versus TMZ use (HR 2.285; CI 1.451–3.598). Decreased HR for death was seen with Asian/Indian ethnicity versus Hispanic ethnicity (HR 0.439; CI 0.223–0.866). On multivariate analysis, KPS less than 70 (HR 3.040; CI 1.402–6.594); extent of surgical resection: subtotal resection or biopsy versus gross total resection (HR 1.560; CI 1.016–2.394 and HR 2.059; CI 1.087–3.903, respectively); RPA class IV and V/VI versus III (HR 3.609; CI 1.404–9.273 and HR 4.384; CI 1.264–15.209, respectively); RT total dose less than 36 Gy versus greater than 54 Gy (HR 3.270; CI 1.685–6.348); and no TMZ use versus TMZ use (HR 2.976; CI 1.207–7.336) were associated with worse outcomes (Table 4).

Subset analysis of only the Hispanic population showed increased HR for death in patients with KPS less than 70 (HR 2.236; CI 1.208–4.140); extent of surgical resection: subtotal resection or biopsy versus gross total resection (HR 3.856; CI 1.623–9.164 and HR 5.284; CI 2.341–11.926, respectively); RPA class IV and V/VI versus III (HR 6.029; CI 0.806–45.079 and HR 16.981; CI 2.192–131.559, respectively); and RT total dose less than 36 Gy versus greater than 54 Gy (HR 9.128; CI 3.612–23.067) (Table 4). On multivariate analysis, extent of surgical resection: subtotal resection or biopsy versus gross total resection (HR 3.011; CI 1.139–7.963 and HR 12.086; CI 2.965–49.269, respectively); RPA class IV versus III (HR 9.327; CI 1.100–79.109); and RT total dose less than 36 Gy versus greater than 54 Gy (HR 5.391; CI 1.162–25.004) were associated with worse outcomes (Table 5). Multivariate analysis limited to the Hispanic population included KPS, extent of surgical resection, RPA class, and RT total dose in the analysis (Table 6). After including these variables together in the Cox regression model, the following were associated with statistically significantly worse OS: both biopsy and subtotal surgical resection compared to gross total resection; RPA Class IV compared to RPA Class III; and RT total dose < 36 Gy compared to RT total dose > 54 Gy.

Subset analysis limited to the 265 patients on TMZ revealed moderate deviations from the results in the entire cohort. Median OS in days was slightly longer in this group (median OS for the TMZ group was 497 days (95% CI: 455–539)). Univariate Cox regression analysis revealed a less significant effect of age (bordering on significant), and no longer showed a significant effect of Asian/Indian ethnicity, tumor bilaterality, or tumor multicentricity on OS

in the TMZ group. Multivariate analysis in the TMZ group included age at diagnosis, KPS, extent of surgical resection, RPA Class, and RT total dose. RPA Class V/VI was no longer associated with significantly worse OS compared to RPA Class III or RT total dose of <36 Gy compared to RT total dose of >54 Gy. However, in the TMZ group, RT total dose between 36–54 Gy was significantly associated with worse OS compared to RT total dose >54 Gy, unlike the pattern seen in the overall cohort.

Discussion:

Recent advances in oncological research have led to interest in personalized medicine. Personalized oncology is evidence-based and involves the use of genomic analysis, targeted drugs, biological and molecular markers, and gender, as well as ethnic variation to determine optimized treatment for patients.[19] Randomized clinical trials (RCT) play an important role in determining the treatment strategy for various diseases. Randomized trial designs typically require and assume a homogenous population. When RCTs are designed to study cancer, selection criteria are usually based on the site and stage of the disease.[20–22] Assuming a homogeneous population in this cohort would result in a limited understanding of the role of individualized criteria such as race and ethnicity. Ultimately, such an approach may miss opportunities to better understand how these patient characteristics affect cancer prognosis and how to optimize treatment in different patient populations with the same disease site and stage. Race and ethnicity have an important impact on molecular pathways in cancer. Differences in race and ethnicity have been shown to contribute to differences in molecular pathways in various human malignancies.[12,23] Furthermore, racial disparities in cancer risk factor, screening, incidence, therapies, and mortality have also been observed in the United States.[24–28]

In the United States, Hispanics represent the largest and fastest growing population, and are a highly heterogeneous group.[29,30] The incidence rate for GBM in the Hispanic population is 2.45 in 100,000.[15] Studies have examined GBM-specific cancer characteristics in the Hispanic population.[13,31–33] However, little is known to date about the survival outcomes of Hispanic patients with GBM. Barnholtz-Sloan and colleagues examined the role of racial and ethnic differences in survival among elderly patients with primary GBM using the population-based Surveillance, Epidemiology and End Results (SEER) Program-Medicare linked database. Although a subset population analysis included the white-Hispanic population, no further analysis for survival was done on this population.[7] Despite these studies, it remains unclear which population-specific outcomes, if any, are to be expected in Hispanic patients that receive radiation therapy.

Some studies have begun to explore this question. In an interesting population study, Aizer and colleagues examined the utilization of radiation therapy in 22,777 patients diagnosed with GBM using the SEER database. Results from their analysis showed that in the entire cohort, the use of radiation was associated with improved OS, as expected. However, a multivariable logistic regression model revealed that the Hispanic population had a significantly higher risk of omitting radiation therapy (odds ratio 1.34, CI 1.19–1.50) compared to the non-Hispanic white population.[10] Possible explanations offered for this association included markers of underserved status, such as lower income and education,

being associated with both non-white ethnicity and omission of RT. This group also proposed the possibility of barriers to effective communication in the patient-physician relationship associated with factors such as age, income, and race. The question remains whether Hispanic GBM patients that receive radiation treatment have similar outcomes compared to white patients, and whether variables such as access to care or toleration of treatment toxicity may play a larger role in this group.

To our knowledge, ours is the first study which focuses on the outcomes of Hispanic patients with newly-diagnosed GBM treated with radiation therapy. The cohort of patients examined in this database includes 428 patients, in which 18% (77 patients) constituted Hispanic patients. Comparing baseline characteristics among the ethnicities (white, black, Hispanic, and Asian/Indian), the cohorts are relatively similar with differences noted in marital status. Initial examination of the patients for OS with Kaplan-Meier curves showed no survival difference between the four groups by ethnicity. The median survival of the Hispanic population was 355 days (approximately 12 months). This value is similar to the reported median survival for all GBM patients.[1] Although the median survivals were not statistically significant across ethnicities, the median OS of the Hispanic cohort was relatively lower. Perhaps a larger, more highly powered study may be able to elucidate differences in survival. Furthermore, as suggested by the Aizer paper, there may be differences in access to medical resources related to the Hispanic population that may affect timing of treatment initiation (including standard of care measures such as surgery, RT, and chemotherapy), compliance to care, and toxicity reporting, and as a result, outcomes. Several studies have explored factors associated with effectiveness of treatment and treatment compliance in the Hispanic population for a variety of health concerns, examining ethnic differences in pain management,[34] adherence in setting of treatment side effects,[35] willingness to discuss issues of treatment tolerability and dissatisfaction,[36] and non-adherence when treated for diseases associated with social stigma.[37] All of these studies acknowledged barriers specific to differences in culture, language, and medical literacy in the experiences of Hispanic patients in receiving optimal treatment, and encourage further emphasis on understanding these topics. Given our unique cohort, we are currently looking into these possibilities, and additional follow-up and research is necessary.

Disparities in healthcare pertaining to Hispanic populations exist; to what extent this affects OS remains unclear. Differences were observed in factors significant for patient outcome in the entire cohort and those in the Hispanic cohort alone. For example, KPS was a significant factor found on multivariate analysis in the whole population, but was not in the Hispanic patients. Despite a larger relative proportion of Hispanic patients in our population, the absolute number in this cohort may be insufficient for examining KPS and OS, further follow up is needed. Extent of resection, RPA class, and RT total dose were significant on multivariate analysis in both the whole population and the Hispanic patients alone. Limitations of this study include its retrospective nature, which could lead to confounding factors related to data collection as well as patient treatment selection bias. Despite this limitation, the baseline characteristics of the patient population were relatively similar. An additional limitation related to the retrospective nature of this study is that the term “Hispanic” encompasses a diverse and widely variable population (among whom are included individuals who could also identify as white, black, or both), thus presenting a

limitation in how patients were classified. Our groupings were based on patient self-reported race/ethnicity, and patients were assigned to the Hispanic group based on their self-identification. Examining further sub-divided groups within the broad category of Hispanic patients will allow for more homogenous cohorts, and could address the limitation of classifying a heterogeneous population into one ethnic group. However, further delineation of Hispanic ethnicity into these sub-categories is difficult given the long history of immigrants in the United States and the ensuing merging of ethnic backgrounds, resulting in rich and complex family trees that continue to be shaped by socioeconomic, sociopolitical, and geographic factors.[30]

In addition, there is recent interest in the molecular characteristics of patients with GBM including IDH-1 status and MGMT methylation status, limited data has been collected, as patients have been routinely screened for the past few years. Although we analyzed molecular characteristics in patients who had this information recorded, the absence of this information in patients seen earlier made this analysis less fruitful than it may be in the future, when patients are more routinely screened for IDH-1 and MGMT status. Further follow-up examining molecular characteristics related to our Hispanic cohort could reveal associations with OS that cannot be adequately assessed at this time.

Conclusion:

GBM is a devastating disease in which outcomes are poor. Radiation therapy is part of the current treatment strategy. Despite an increasing interest in personalized medicine, very little is currently known about the outcomes of Hispanic patients with newly diagnosed GBM treated with radiation. In our study population, no differences in survival were seen between the different ethnicities. Hispanic patients had different prognostic factors compared to the entire cohort. Future studies focusing on biological and social characteristics associated with race and ethnicity may help determine how they affect cancer prognosis, with the goal of optimizing treatment in different patient populations with the same disease site and stage.

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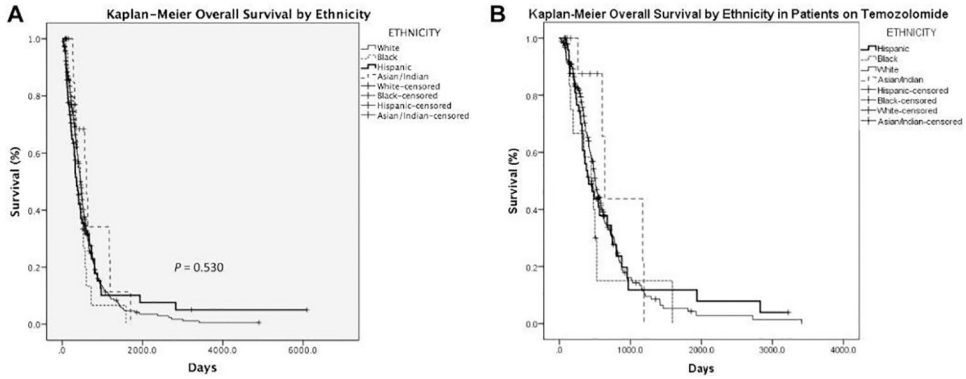

Figure 1:
Kaplan-Meier curves to assess Overall Survival by Ethnicity.

Table 1:

Baseline Characteristics

	Total	%	White	%	Black	%	Hispanic	%	Asian/Indian	%	p-Value
Age at Diagnosis (N)	**428**		**313**	**73.1**	**21**	**4.9**	**77**	18.0	17	4.0	0.379
<50	102	23.8	74	23.6	7	33.3	15	19.5	6	35.3	
≥50	326	76.2	239	76.4	14	66.7	62	80.5	11	64.7	
Gender (N)	**428**		**313**	**73.1**	**21**	**4.9**	**77**	**18.0**	**17**	**4.0**	0.911
Male	247	57.7	181	57.8	11	52.4	46	59.7	9	52.9	
Female	181	42.3	132	42.2	10	47.6	31	40.3	8	47.1	
Marital Status (N)	**425**		**311**	**73.2**	**21**	**4.9**	**76**	**17.9**	**17**	**4.0**	**0.001**
Married	299	70.4	235	75.6	9	42.9	40	52.6	15	88.2	
Unmarried	126	29.6	76	24.4	12	57.1	36	47.4	2	11.8	
KPS (N)	**428**		**313**	**73.1**	**21**	**4.9**	**77**	**18.0**	**17**	**4.0**	0.459
≥70	346	80.8	258	82.4	16	76.2	58	75.3	14	82.4	
<70	82	19.2	55	17.6	5	23.8	19	24.7	3	17.6	
Extent of Surgical Resection (N)	**302**		**217**	**71.9**	**16**	**5.3**	**57**	**18.9**	**12**	**4.0**	0.411
Gross Total Resection	193	63.9	139	64.1	13	81.3	32	56.1	9	75.0	
Subtotal Resection	45	14.9	29	13.4	2	12.5	13	22.8	1	8.9	
Biopsy	64	21.2	49	22.6	1	6.3	12	21.1	2	16.7	
RPA Class (N)	**366**		**264**	**72.1**	**18**	**4.9**	**68**	**18.6**	**16**	**4.4**	0.203
III	38	10.4	30	11.4	1	5.6	5	7.4	2	12.5	
IV	224	61.2	163	44.5	15	4.1	36	52.9	10	62.5	
V/VI	104	28.4	71	26.9	2	11.1	27	39.7	4	25.0	
RT Technique (N)	**421**		**308**	**73.2**	**20**	**4.8**	**76**	**18.1**	**17**	**4.0**	**0.001**
IMRT	231	54.9	169	54.9	12	60.0	38	50.0	12	70.6	
3D CRT	170	40.4	133	43.2	7	35.0	26	34.2	4	23.5	
2D	20	4.8	6	1.9	1	5.0	12	15.8	1	5.9	
RT Total Dose (N)	**428**		**313**	**73.1**	**21**	**4.9**	**77**	**18.0**	**17**	**4.0**	0.617
<36 Gy	42	9.8	32	10.2	2	9.5	8	10.4	0	0	
36–54 Gy	41	9.6	31	9.9	0	0	9	11.7	1	5.9	
>54 Gy	345	80.6	250	29.9	19	90.5	60	77.9	16	94.1	
Laterality (N)	**399**		**290**	**72.7**	**20**	**5.0**	**73**	**18.3**	**16**	**4.0**	0.973
Unilateral	331	83.0	241	83.1	17	85.0	60	82.2	13	81.3	
Bilateral	68	17.0	49	16.9	3	15.0	13	17.8	3	18.8	
Multicentricity (N)	**399**		**290**	**72.7**	**20**	**5.0**	**73**	**18.3**	**16**	**4.0**	0.278
No	314	78.7	222	76.6	17	85.0	63	86.3	12	75.0	
Yes	85	21.3	68	23.4	3	15.0	10	13.7	4	25.0	
IDH-1 Status (N)	**93**		**68**	**73.1**	**3**	**3.2**	**16**	**17.2**	**6**	**6.5**	0.406
Negative	87	93.5	63	92.6	3	100	16	100	5	83.3	

	Total	%	White	%	Black	%	Hispanic	%	Asian/Indian	%	p-Value
Positive	6	6.5	5	7.4	0	0	0	0	1	16.7	
MGMT Status (N)	**65**		**46**	**70.8**	**2**	**3.1**	**12**	**18.5**	**5**	**7.7**	0.259
Unmethylated	38	58.5	28	60.9	2	100	7	58.3	1	20.0	
Methylated	27	41.5	18	29.1	0	0	5	41.7	4	80.0	
Temozolomide (N)	**286**		**208**	**72.7**	**15**	**5.2**	**51**	**17.8**	**12**	**4.2**	0.216
Yes	265	92.7	191	91.8	13	86.7	50	98.0	11	91.7	
No	21	7.3	17	18.2	2	13.3	1	2.0	1	8.3	

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Table 2

Kaplan Meier Median OS by Ethnicity

	Days	95% CI
White	457	414–500
Black	449	268–630
Hispanic	355	275–435
Asian	602	495–709
Overall	450	410–490

Table 3:

Univariate Cox Regression Analysis for Overall Survival Over Entire Cohort

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
Age at Diagnosis				
<50	1			Reference
≥50	1.826	1.409	2.368	**0.001**
Gender				
Male	1			Reference
Female	0.989	0.799	1.223	0.918
Ethnicity				
White	1			Reference
Black	1.192	0.738	1.926	0.472
Hispanic	1.039	0.781	1.384	0.791
Asian/Indian	0.675	0.358	1.270	0.222
Marital Status				
Married	1			Reference
Unmarried	1.117	0.882	1.415	0.358
KPS				
≥70	1			Reference
<70	3.23	2.452	4.262	**0.001**
Extent of Surgical Resection				
Gross Total Resection	1			Reference
Subtotal Resection	1.698	1.182	2.440	**0.004**
Biopsy	2.992	2.180	4.107	**0.001**
RPA Class				
III	1			Reference
IV	2.357	1.511	3.675	**0.001**
V/VI	7.815	4.816	12.681	**0.001**
RT Technique				
IMRT	1			Reference
3D CRT	1.417	1.136	1.766	**0.002**
2D	4.033	2.452	6.633	**0.001**
RT Total Dose				
<36 Gy	4.526	3.202	6.396	**0.001**
36–54 Gy	1.787	1.158	2.757	**0.009**
>54 Gy	1			Reference
Laterality				
Unilateral	1			Reference
Bilateral	1.317	0.983	1.764	0.065
Multicentricity				

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
No	1			Reference
Yes	1.311	0.995	1.727	0.054
IDH-1 Status				
Negative	26.362	0.296	2351.589	0.153
Positive	1			Reference
MGMT Status				
Unmethylated	1.136	0.338	3.816	0.836
Methylated	1			Reference
Temozolomide				
Yes	1			Reference
No	2.285	1.451	3.598	**0.001**

Table 4:

Multivariate Cox Regression Analysis for Overall Survival Over Entire Cohort

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
Age at Diagnosis				
<50	1			Reference
≥50	1.045	0.627	1.743	0.865
Ethnicity				
White	1			Reference
Black	0.790	0.372	1.677	0.540
Hispanic	1.035	0.657	1.632	0.881
Asian/Indian	0.501	0.179	1.405	0.501
KPS				
≥70	1			Reference
<70	3.702	1.608	8.520	**0.002**
Extent of Surgical Resection				
Gross Total Resection	1			Reference
Subtotal Resection	1.532	0.992	2.366	0.054
Biopsy	2.209	1.129	4.320	**0.021**
RPA Class				
III	1			Reference
IV	3.178	1.223	8.255	**0.018**
V/VI	3.499	0.979	12.508	0.054
RT Technique				
IMRT	1			Reference
3D CRT	0.618	0.363	1.055	0.078
2D	2.261	0.278	18.402	0.446
RT Total Dose				
<36 Gy	3.978	1.836	8.621	**0.001**
36–54 Gy	1.214	0.651	2.264	0.542
>54 Gy	1			Reference
Laterality				
Unilateral	1			Reference
Bilateral	1.468	0.908	2.372	0.117
Multicentricity				
No	1			Reference
Yes	1.130	0.736	1.735	0.576
Temozolomide				
Yes	1			Reference
No	3.908	1.526	10.008	**0.004**

Table 5:

Univariate Cox Regression Analysis for Overall Survival Over Hispanic Population

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
Age at Diagnosis				
<50	1			Reference
≥50	1.922	0.968	3.817	0.062
Gender				
Male	1			Reference
Female	1.351	0.801	2.278	0.260
Marital Status				
Married	1			Reference
Unmarried	1.407	0.836	2.370	0.199
KPS				
≥70	1			Reference
<70	2.236	1.208	4.140	**0.010**
Extent of Surgical Resection				
Gross Total Resection	1			Reference
Subtotal Resection	3.856	1.623	9.164	0.002
Biopsy	5.284	2.341	11.926	**<0.001**
RPA Class				
III	1			Reference
IV	6.029	0.806	45.079	0.080
V/VI	16.981	2.192	131.559	**0.007**
RT Technique				
IMRT	1			Reference
3D CRT	1.563	0.877	2.784	0130
2D	3.026	1.411	6.487	**0.004**
RT Total Dose				
<36 Gy	9.128	3.612	23.067	**<0.001**
36–54 Gy	0.704	0.251	1.975	0.505
>54 Gy	1			Reference
Laterality				
Unilateral	1			Reference
Bilateral	0760	0.370	1.562	0.455
Multicentricity				
No	1			Reference
Yes	1.581	0.705	3.543	0.266

Table 6:

Multivariate Cox Regression Analysis for Overall Survival Over Hispanic Population

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
KPS				
≥70	1			Reference
<70	1.153	0.795	12.628	0.102
Extent of Surgical Resection				
Gross Total Resection	1			Reference
Subtotal Resection	2.948	1.111	7.825	**0.030**
Biopsy	15.890	3.292	76.696	**0.001**
RPA Class				
III	1			Reference
IV	9.094	1.046	79.095	**0.045**
V/VI	4.041	0.457	35.762	0.209
RT Technique				
IMRT	1			Reference
3D CRT	0.656	0.257	1.673	0.377
2D	0.482	0.114	2.035	0.321
RT Total Dose				
<36 Gy	9.611	1.420	65.039	**0.020**
36–54 Gy	0.978	0.297	3.220	0.970
>54 Gy	1			Reference

Table 7:

Kaplan-Meier median Overall Survival by Ethnicity in Patients on Temozolomide

	Days	95% CI
White	507	460–554
Black	449	244–654
Hispanic	411	254–568
Asian	638	565–711
Overall	497	455–539

Table 8:

Univariate Cox Regression Analysis for Overall Survival in Patients on Temozolomide

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
Age at Diagnosis				
<50	1			Reference
≥50	1.399	0.973	2.011	.070
Gender				
Male	1			Reference
Female	0.985	0.740	1.310	.917
Ethnicity				
Hispanic	1			Reference
Black	1.343	0.663	2.720	.413
White	0.999	0.689	1.446	.994
Asian/Indian	0.599	0.234	1.533	.285
Marital Status				
Married	1			Reference
Unmarried	1.204	0.873	1.659	.258
KPS				
≥70	1			Reference
<70	3.680	2.551	5.308	**<.0001**
Extent of Surgical Resection				
Gross Total Resection	1			Reference
Subtotal Resection	1.515	1.014	2.264	**.043**
Biopsy	3.051	1.958	4.754	**<.0001**
RPA Class				
III	1			Reference
IV	2.398	1.167	4.927	**.017**
V/VI	7.314	3.391	15.774	**<.0001**
RT Total Dose				
<36 Gy	4.457	2.673	7.432	**<.0001**
36–54 Gy	1.750	1.015	3.016	**.044**
>54 Gy	1			Reference
Laterality				
Unilateral	1			Reference
Bilateral	1.327	0.892	1.973	.162
Multicentricity				
No	1			Reference
Yes	1.247	0.861	1.807	.243
IDH-1 Status				
Negative	26.362	0.296	2351.589	.153

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
Positive	1			Reference
MGMT Status				
Unmethylated	1.136	0.338	3.816	.836
Methylated	1			Reference

Table 9:

Multivariate Cox Regression Analysis for Overall Survival in Patients on Temozolomide

Variable	Hazard Ratio	95% CI (Lower)	95% CI (Upper)	p-value
Age at Diagnosis				
<50	1			Reference
≥50	1.036	0.630	1.705	.888
KPS				
≥70	1			Reference
<70	4.178	1.905	9.160	**<.0001**
Extent of Surgical Resection				
Gross Total Resection	1			Reference
Subtotal Resection	1.610	1.063	2.438	**.024**
Biopsy	2.798	1.478	5.296	**.002**
RPA Class				
III	1			Reference
IV	2.396	0.956	6.003	.062
V/VI	2.014	0.560	7.248	.284
RT Total Dose				
<36 Gy	1.345	0.748	2.417	.322
36–54 Gy	2.795	1.443	5.415	**.002**
>54 Gy	1			Reference