The Majority of Primary Glioblastoma Long-Term Survivors are Not IDH-1 Mutation-Positive

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Introduction

It is estimated that 3-5% of glioblastoma (GBM) patients are long-term survivors (LTS), as defined by survival of more than 3 years. Given the improved survival conferred by IDH-1 mutations and the fact these mutations are detected in 12% of newly diagnosed GBM cases, could long-term survivorship be explained by IDH-1 mutation status? The objective of our study was to assess what proportion of our GBM LTS had IDH-1 mutations.

Table 1. Characteristics of 40 long-term newly diagnosed GBM patients.

Variables	N (%)
Number of patients	40
Age at diagnosis, years	
mean (SD)	49.9 (13.2)
median [IQR]	50 [40-60]
Gender, N (%)	
female	18 (45.0)
male	22 (55.0)
KPS at diagnosis	
mean (SD)	86 (9.0)
median [IQR]	80 [80-90]
Tumor size in centimeters	
1-3	7 (18.9)
3-4	6 (17.1)
4-6	16 (43.2)
>6	8 (21.6)
missing	3 (7.5)
TREATMENT	
Extent of resection	
biopsy	6 (15.4)
partial	4 (10.3)
near/gross total	29 (72.5)
Radiation	
yes	39 (97.5)
no	1 (2.5)
Temozolomide	
yes	38 (95.0)
no	2 (5.0)
Dendritic cell vaccine	
yes	11 (27.5)
no	29 (72.5)

Methods

The records of 453 newly-diagnosed adult GBM patients treated at a single institution from January 2004 to November 2011 were retrospectively reviewed for patients who survived at least 36 months following their initial surgery. Descriptive statistics for clinical characteristics, treatments received, and tumor biomarkers were reported. Kaplan-Meier survival estimates were provided for progression -free survival (PFS) and overall survival (OS).

Results

Forty (8.8%) LTS GBM patients were identified, with a median age of 50 years old and a median postoperative Karnofsky Performance Score (KPS) of 80. Most patients underwent near/gross-total resection (72.5%), postoperative radiation (97.5%), and adjuvant temozolomide (95%). Eleven (27.5%) patients received dendritic cell vaccine therapy. PFS rates at 12, 36, and 48 were 67.5%, 40%, and 32.7%, respectively. Median OS has not yet been reached; however, the survival rate at 48 months was 62.1%.

Of the 35 patients with available tumor samples, only 8 (22.9%) had IDH-1 mutations. There was no significant difference in time to progression between IDH-1 mutation patients and patients with wild type IDH-1 (46.6 vs. 26.3 months, log rank p=.45).

Table 2. Median survival, survival rates, and 95% confidence intervals (CI).

	PFS	OS
Median survival (CI)*	27.6 (13.6-45.5)	not reached*
Survival rates, % (CI)		
6-month	75.0 (58.5-85.7)	100
12-month	67.5 (50.7-79.7)	100
18-month	57.5 (40.8-71.0)	100
36-month	40.0 (25.0-54.6)	100
48-month	32.7 (18.2-48.1)	62.1 (42.4-76.7)

*14 of 40 patients are deceased; 26 patients are censored.

Table 3. Biomarkers of 40 long-term newly diagnosed GBM patients.*

Variable	N (%)
PTEN	
loss	14 (50.0)
retained	14 (50.0)
MGMT	
20% or greater	5 (17.9)
less than 20%	23 (82.1)
IDH-1	
negative	27 (77.1)
positive	8 (22.9)

* PTEN, MGMT, and IDH-1 data was not available in 12, 12, and 5 patients, respectively, of the total 40 patients analyzed.

Table 4. Progression and overall survival by IDH-1 mutation status.

	Progression Free Survival IDH-1 wild type		Overall Survival IDH-1 wild type	
	no N=8 (22.9%)	yes N=27 (77.1%)	no N=8 (22.9%)	yes N=27 (77.1%)
Median survival (CI)	46.6 (3.3-84.0)	26.3 (7.2-45.5)	not reached	not reached
Survival rates, % (CI)				
12-month	87.5 (38.7-98.1)	66.6 (45.7-81.1)	100	100
24-month	75 (31.5-93.0)	51.9 (31.9-68.5)	100	100
36-month	50 (15.2-77.5)	40.7 (22.5-58.2)	100	100
48-month	50 (15.2-77.5)	29.1 (12.3-48.3)	75 (31.5-93.1)	56.3 (31.9-74.9)

Conclusions

Less than a quarter of our patients' long-term survivorship was associated with favorable IDH-1 status. Therefore, IDH-1 status does not explain the majority of long-term survivorship in the temozolomide era.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe what defines a glioblastoma long-term survivor, 2) Describe what percentage of newly diagnosed glioblastoma patients will become long-term survivors, 3) Describe the characteristics of glioblastoma long-term survivors, and 4) Describe the impact of IDH-1 mutation-positive status in determining glioblastoma long-term survivorship.

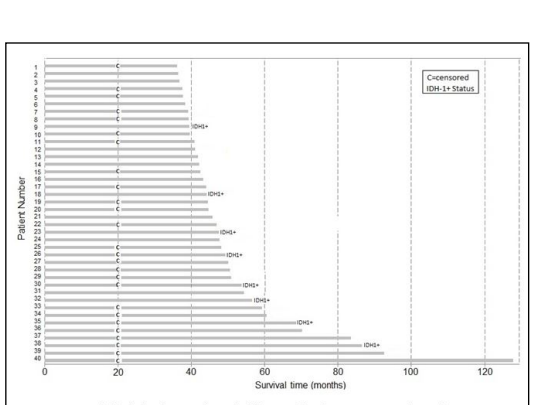

Figure 1. Bar graph depicting the overall survival (in months) of our GBM LTS. Those who are IDH-1 positive are noted.

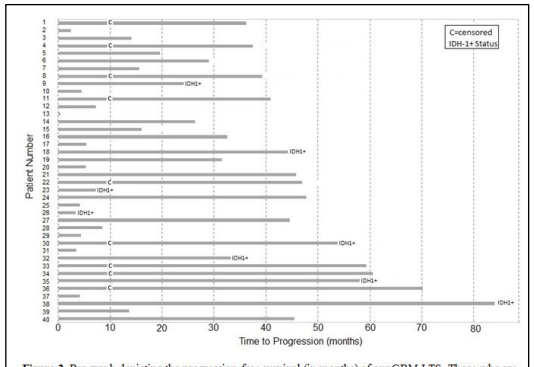

Figure 2. Bar graph depicting the progression-free survival (in months) of our GBM LTS. Those who are IDH-1 positive are noted.