

**PATIENT REPORT**

**Patient:**  
**Sex:**  
**DOB:**  
**Tissue Received:**  
**Date Reported:**  
**Treating Physician:**

**Medical Record/Patient #:**  
**Date of Surgery:**  
**Specimen ID/Block ID:**  
**Client:**  
**Submitting Pathologist:**  
**Additional Recipient:**

**ASSAY DESCRIPTION**

**DecisionDx-GBM<sup>®</sup>** brain cancer assay uses RT-PCR to determine the expression of a panel of 12 genes (3 control) in tumor tissue. The **DecisionDx-GBM** score is calculated from the gene expression results. The score range is uncapped.

**RESULTS**

**DecisionDx-GBM score =**

**Quintile Rank = 1**

**Patient's with a DecisionDx-GBM score of , which lies within the 1st quintile, have a likelihood of survival to 2 years (when treated with radiation and temozolomide alone) of 74% with a median survival of 87 months and median progression free survival not reached.**

**Test Results should be interpreted using the Clinical Experience information contained in this report which is derived from clinical studies involving patient populations with specific clinical features as noted in section titled Clinical Experience. These results have not been validated in patients with clinical features different from those described.**

**CLINICAL EXPERIENCE**

The following results are from two clinical validation studies (Study 1, n=68 treated with standard of care; and Study 2, n=101 treated with radiation plus concurrent and adjuvant temozolomide), both of which included patients with newly diagnosed, grade IV GBM, all of whom were treated with standard of care (reference: Colman et al, in press). The results of the second validation study (n=101) specifically demonstrated DecisionDx-GBM to be an independent predictor of overall survival in patients with grade IV GBM in patients treated with radiation plus concurrent and adjuvant temozolomide.

**Multi-variate analysis has shown DecisionDx-GBM to be an independent predictor of overall survival relative to age, performance status (KPS), and MGMT methylation.**

**RAW DATA AND CALCULATION OF DECISIONDX-GBM SCORE**

The optimized molecular model, which included combining both validation studies (n=169) and weighting each gene according to the strength of association with survival was also found to be independent of known clinical factors (ie: age and performance score) and the investigational use of MGMT methylation in multivariate analyses.

Gene symbol	Gene name	$\Delta C_t$	$\beta$ -value coefficient	$\Delta C_t \times \beta$
AQP1	aquaporin 1		0.15	0
CHI3L1	Chitinase 3-like 1/YKL-40		0.12	0
EMP3	epithelial membrane protein 3		0.14	0
GPNMB	Glycoprotein nmb		0.21	0
IGFBP2	insulin-like growth factor binding protein 2		0.23	0
LGALS3	galectin 3		0.14	0
OLIG2*	oligodendrocyte lineage transcription factor 2		-0.15	0
PDPN	Podoplanin		0.19	0
RTN1*	reticulon 1		-0.2	0
DecisionDx-GBM Score =				0
Control Genes = EEF1A1, GUSB, RPS27				

\* = OLIG2 and RTN1 over-expression associated with improved outcome

$\Delta C_t$  = Calculated for each gene by comparison with the average of the Ct values for 3 control genes

$\beta$  -value coefficient = derived from Cox analysis

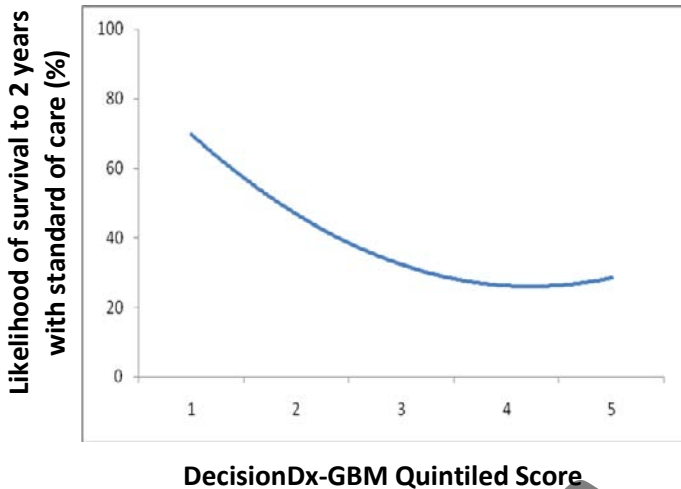
**LABORATORY DIRECTOR: John F. Stone, PhD FACMG**

St. Joseph's Hospital and Medical Center, CLIA# 03D0526691

This test was developed and its performance characteristics determined by Castle Biosciences Inc under its work-for-hire master services agreement with St. Joseph's Hospital DNA diagnostic Laboratories. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA) and as such is not required to go through pre-market FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. The results are adjunctive to the ordering physician's workup.

## BACKGROUND INFORMATION

The line graph below shows the logarithmic trendline for the quintiled patient data.



The table below shows results from Study 2 (n=101) in which MGMT methylation status was performed in addition to the DecisionDx-GBM test. In multivariate analysis the DecisionDx-GBM test was found to be an independent variable whereas MGMT methylation status was not.

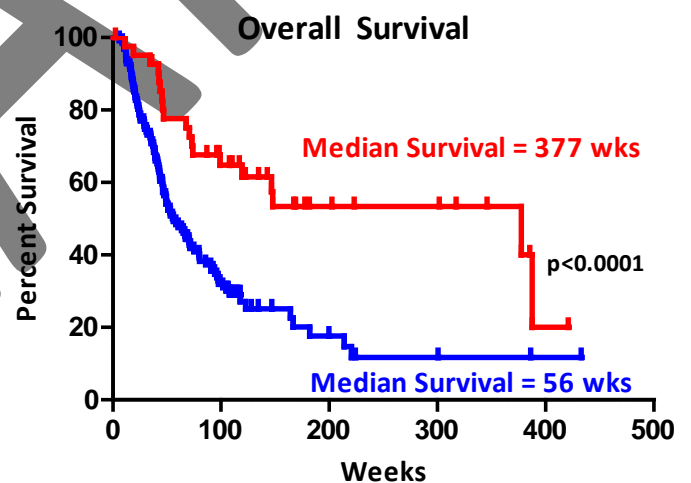
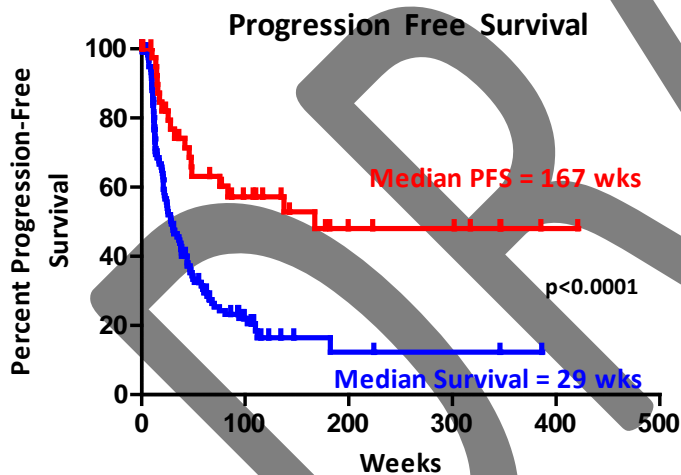
### Log Rank Analysis

	Overall Survival
DecisionDx-GBM	p= 0.0096
MGMT status	p=0.0556

### Cox Proportional Multivariate Analysis

	Overall Survival	
	HR	p-value
DecisionDx-GBM	3.3	0.0055
MGMT status	1.9	0.0602

Clinical database for patients in Study 2 and 3 was updated March 31, 2009. Kaplan-Meier curve on left shows status for progression free survival and Kaplan-Meier curve on right shows status for overall survival. Patients were divided into 2 groups based upon results from recursive partitioning analysis.



## REFERENCE LIST

- Colman, et al. 2006. Meta-analysis of gene expression profiling data from glioblastoma tumor samples identifies a robust Multigene classifier predictive of survival. Proc Amer Assoc Cancer Res, Volume 47, Abstract # 5688.
- Colman, et al. 2007. A robust Multigene classifier predictive of survival in patients with newly diagnosed glioblastoma. Proc Amer Assoc Cancer Res. Vol , Abstract #2700.
- Aldape, et al. 2006. Meta-analysis of gene expression profiling data from glioblastoma tumor samples identifies a robust multigene classifier predictive of survival. Journal of the Society for Neuro-Oncology. Abstract GE-01.
- Colman, et al. 2009. A multigene predictor of outcome in glioblastoma. Neuro-Oncology, accepted.

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