Differences in Biomarker Expression in GBM Patients with Early Progression after Surgery

Joshua Palmer MD, Jianliang Li MD, Lawrence Kenyon MD, David W. Andrews, MD, Lyndon Kim MD, Jon Glass MD, Maria Werner-Wasik MD, Wenyin Shi MD, PhD

Jefferson Medical College of Thomas Jefferson Hospital, Philadelphia, PA

Purpose

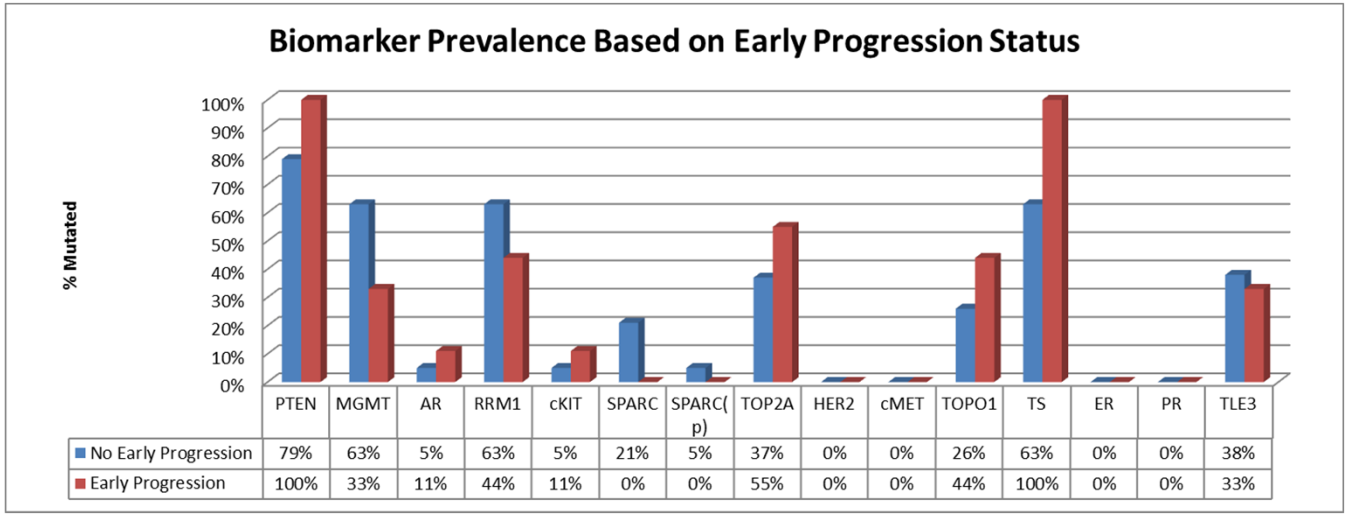
- Glioblastoma Multiforme (GBM) is locally aggressive
- GBM is the most common primary brain tumor in adults
- Surgery followed by temozolomide and radiotherapy are the standard of care
- Attempts have been made to increase radiation dose, pursue more aggressive chemotherapy, or add targeted therapy
- Biomarker expression may help individualize treatment decisions

Methods

- 28 newly diagnosed GBM patients
- Treatment between January 2012 and May 2013
- Tumor profiling provided by Caris Life Sciences, Inc.
- Immunohistochemistry, FISH, CISH, MGMT promoter methylation and NextGen SEQ (Illumina TruSeq) were performed on formalin-fixed, paraffin-embedded tumor samples in a CLIA certified lab
- MRI imaging was performed on post-operative day 1 and at the time of CT simulation for radiation treatment planning
- Early Progression (EP) was defined as either new enhancing lesions or >25% increase in the T1 post-contrast enhancement.
- Two sided Fisher Exact Tests were used on contingency tables

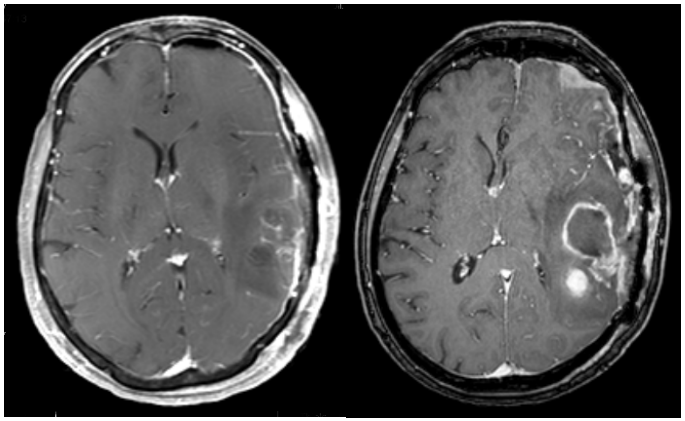
Results

- Median time between MRI imaging 20 days
- 28.6% of patients had EP
- The genes more frequently expressed in EP group:
  - PTEN, p=NS
  - AR, p=NS
  - cKIT, p=NS
  - TOP2A, p=NS
  - TOPO1 p=NS
  - TS, p=0.06
- The genes more frequently expressed in the non-EP group
  - MGMT hypermethylation
  - RRM1
  - SPARC monoclonal
  - SPARC polyclonal



	PTEN	MGMT	AR	RRM1	cKIT	SPARC	SPARC(p)	TOP2A	HER2	cMET	TOPO1	TS	ER	PR	TLE3
No Early Progression	79%	63%	5%	63%	5%	21%	5%	37%	0%	0%	26%	63%	0%	0%	38%
Early Progression	100%	33%	11%	44%	11%	0%	0%	55%	0%	0%	44%	100%	0%	0%	33%

Example of Early Progression



Depicted above are A) the post-operative and B) Treatment planning MRI axil images revealing a new T1 post-contrast enhancing mass posterior to the resection cavity

Patient Characteristics			
Age at Diagnosis(years)		Location (n)	
Average	60	*Frontal*	18.00
Range	43-86	*Parietal*	7.00
Male (%)	26 (62)	*Temporal*	14.00
Female (%)	16(38)	*Occipital*	1.00
Extent of Surgery		*Basal Ganglia*	3.00
Gross total (%)	27	*Cerebellar*	1.00
Subtotal (%)	73	Tumor Size (cc)	
Tumor Histology (n)		*Average*	35.9
Glioblastoma	39	*Range*	8.8-61.4
Gliosarcoma	2	Avg. FLAIR extent(cc	110.2
Clear Cell Glioblastoma	1		

Conclusions

- There are different gene expression profiles in patients with EP
- This may lead to differing biology, aggressiveness and early treatment decisions
- This data will be confirmed in a validation set

For more information:
Joshua. Palmer@jeffersonhospital.org