

Journal of Clinical Oncology, 2011 ASCO Annual Meeting Proceedings (Post-Meeting Edition).  
Vol 29, No 18\_suppl (June 20 Supplement), 2011: LBA2000  
© 2011 American Society of Clinical Oncology

## RTOG 0525: Molecular correlates from a randomized phase III trial of newly diagnosed glioblastoma.

K. D. Aldape, M. Wang, E. P. Sulman, M. Hegi, H. Colman, G. Jones, A. Chakravarti, M. P. Mehta, D. W. Andrews, L. Long, K. Diefes, L. Heathcock, R. Jenkins, C. J. Schultz, M. R. Gilbert and Radiation Therapy Oncology Group

University of Texas M. D. Anderson Cancer Center, Houston, TX; Radiation Therapy Oncology Group, Philadelphia, PA; University of Lausanne Hospitals (CHUV), Lausanne, Switzerland; University of Utah, Salt Lake City, UT; Oncomethylome, Durham, NC; Arthur G. James Cancer Hospital, The Ohio State University Medical Center, Columbus, OH; Northwestern University, Chicago, IL; Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA; Mayo Clinic, Rochester, MN; Medical College of Wisconsin, Milwaukee, WI; M. D. Anderson Cancer Center, Houston, TX

### Abstract Disclosures

### Abstract

#### LBA2000

**Background:** Formalin-fixed, paraffin embedded GBM tumor tissue, adequate for conventional MGMT methylation analyses, was required for entry onto the RTOG 0525 clinical trial. **Methods:** Four prognostic biomarkers were evaluated on a training set of 220 retrospectively obtained GBM samples, consisting of IDH1 mutation, the glioma-CpG island methylator phenotype (G-CIMP), a microarray-based mRNA panel and a novel MGMT promoter methylation assay. For each biomarker, 2 (IDH1 and mRNA) or 3 subgroups (G-CIMP and MGMT) were defined based on associations with overall survival. All combinations (36 possible) of each of the 4 biomarker-derived subgroups were then defined and compared with survival data and then consolidated into 4 risk groups. Once created in the training set, this model was applied to the RTOG 0525 samples (n=763) for external validation. **Results:** Application of the molecular risk classification to RTOG 0525 samples (left table) showed a highly significant survival association ( $p < 0.001$ ). When compared to the recursive partitioning analysis (RPA, table on right), this composite molecular classifier better identified patients with long term survival and appears to improve resolution by revealing an additional distinct risk group. The molecular classifier was prognostic in each of the treatment arms individually. **Conclusions:** Four distinct biomarkers or biomarker panels were tested in GBM. These biomarkers were compared with clinical outcome in a training set to optimize a method to combine them into a classifier. This classifier was then validated on a large sample set from a large phase III clinical trial. This composite panel may represent an improvement over the existing RPA with respect to risk stratification of patients for GBM. Additionally, it has the potential to impact future clinical trial designs and provide enhanced opportunities for personalization of therapy for GBM. Support: NCI U10 CA2121661, U10 CA37422, P50 CA127001.

Molecular risk classification	Molecular data			RPA (clinical) data			
	N (%)	Median survival, months	2-year survival %	RPA	N (%)	Median survival, months	2-year survival %
1	106 (14)	26	53%	3	141 (18)	23	48%
2	157 (20)	20	39%	4	461 (60)	16	28%
3	227 (30)	15	27%	5	161 (21)	11	18%
4	273 (36)	12	17%				

Abstract presentation from the 2011 ASCO Annual Meeting