Comparison of molecular alteration in glioblastoma tumors from old and young patients

Jooane Xiu, 2Sherie D Ferguson, 2Sandeep K. Reddy, 2Santosh Kesari, 2Stephanie E. Weiss, 2Raymond J. Hohl, 2Geoffrey Barger, 2Amy B. Heilberger

1Caris Life Sciences, Phoenix, AZ; 2University of Texas MD Anderson Cancer Center, Houston, TX; 3John Wayne Cancer Institute at Providence, Santa Monica, CA; 4Fox Chase Cancer Center, Philadelphia, PA; 5Penn State Hershey Cancer Inst, Hershey, PA; 6Karnamors Cancer Institute, Detroit, MI

Abstract #2056

Background: GBM patients (~170 yr old or younger have a poorer prognosis than younger pts. IDH/2 mutations are more prevalent in younger GBM pts. and confer a more favorable prognosis. We compared molecular alterations between younger pts. (YP: 18-< age 45), and older pts. (OP: age >70), with additional stratification for wild type IDH2/1 status.

Methods: GBM tumors submitted for tumor profiling between 2009 and Jan 2016 were tested with NextGen sequencing (SEQ), immunohistochemistry (IHC), fluorescent in-situ hybridization (FISH), fragment analysis (FA) and promoter methylation (Me). Retrospective analysis was performed on 375 GBM's (YP = 197, OP = 178). Pediatric tumors were excluded. Chi-square was used for exploratory analyses and significance was defined as p < 0.05. Given the nature of this exploratory study, p values were not adjusted for multiple testing.

Results: Alterations including overexpression of ALK (29% vs. 4%), RRM1 (47% vs. 32%) and mutations of ATRX (73% vs. 1%), BRAF (0.3% vs. 1.7%), IDH2 (24% vs. 78%) or IDH1 (0% vs. 0%), PTPN11 (6.6% vs. 1%) and TP53 (58% vs. 26%) were significantly more prevalent in YP (N = 197). In contrast, Pten mutation was significantly more frequent in OP (26% vs. 13%). Pten loss by IHC was equal between YP and OP (22% vs. 21%). Pts. with known wild type IDH2/1 status were compared between YP and OP (N = 72 and 95). Significantly higher expression of TOPO1 was seen in YP (61% vs. 45%) while MGMT-1 was less common in YP (25% vs. 48%). The differences in ALK IHC (27% vs. 4.5%), mutations of BRAF (12% vs. 1%), PDRGA (4% vs. 0), PTPN11 (71% vs. 1%) and TP53 (42% vs. 25%) were significant. K-Ras and PDRGA amplifications were seen in 2 out of 3 tumors from OP with wild type IDH2/1 while no K-Ras or PDRGA amplification was seen in YP (0%). No significant differences were seen in OP vs. YP for EGFRvIII (12%-14%), PD-L1 expression on tumor cells (19% vs. 8.3%) or PD-1 expression on Tl (42% vs. 54%).

Conclusions: Significant molecular differences were seen between older and younger GBM pts. Alterations seen in OP, including Pten mutation and cK-Ras/PGRGA co-amplification were previously associated with recurrent tumors and poor survival, and may underlie the poorer prognosis observed in OP. These results suggest and may guide which pts. will benefit from targeted therapies in future studies.

Background

• The prognostic benefit that a younger age confers has been well described in the literature and has been attributed to several factors including: higher pre-treatment EFS, greater likelihood of aggressive surgical resection, increased eligibility for clinical trials and a more robust social support system.

• More recently the age related molecular differences in GBM patients have been highlighted. For instance, IDH 1/2 mutation is more prevalent in younger patients and confers a more favorable prognosis.

• Further, TCGA subtyped GBM into four molecular classes and reported significant molecular differences based on patient age.

• The aim of this study is to investigate biomarker data collected for molecular profiling of glioblastoma tumors from old and young patients, and confers a more favorable prognosis.

• The prognostic benefit that a younger age confers has been well described in the literature and has been attributed to several factors including: higher pre-treatment EFS, greater likelihood of aggressive surgical resection, increased eligibility for clinical trials and a more robust social support system.

• More recently the age related molecular differences in GBM patients have been highlighted. For instance, IDH 1/2 mutation is more prevalent in younger patients and confers a more favorable prognosis.

• Further, TCGA subtyped GBM into four molecular classes and reported significant molecular differences based on patient age.

• The aim of this study is to investigate biomarker data collected for molecular profiling of glioblastoma tumors from old and young patients, and confers a more favorable prognosis.

• The prognostic benefit that a younger age confers has been well described in the literature and has been attributed to several factors including: higher pre-treatment EFS, greater likelihood of aggressive surgical resection, increased eligibility for clinical trials and a more robust social support system.

• More recently the age related molecular differences in GBM patients have been highlighted. For instance, IDH 1/2 mutation is more prevalent in younger patients and confers a more favorable prognosis.

• Further, TCGA subtyped GBM into four molecular classes and reported significant molecular differences based on patient age.

• The aim of this study is to investigate biomarker data collected for molecular profiling of glioblastoma tumors from old and young patients, and confers a more favorable prognosis.