Title

ACTR-35. A STUDY OF RACE AND SOCIOECONOMIC STATUS IMPACTING THERAPEUTIC CLINICAL TRIAL ENROLLMENT IN ADULT GLIOMAS PATIENTS

Journal

Neuro-oncology, 21(Suppl 6)

ISSN

1522-8517

Authors

Morshed, Ramin
Reihl, Sheantel
Kakaizada, Sofia
et al.

Publication Date

2019-11-01

Peer reviewed

New York, NY, USA, [11]Department of Neurology, UCLA, Los Angeles, CA, USA, [12]University of California Los Angeles, Los Angeles, CA, USA, [13]Oncoceutics, Inc., Philadelphia, PA, USA, [14]Brigham and Women's Hospital, Boston, MA, USA, [15]Columbia University Irving Medical Center, New York, USA, [16]Dana-Farber Cancer Institute, Boston, MA, USA

H3 K27M-mutant gliomas often manifest as midline gliomas, have a dismal prognosis, and have no established or effective treatments at recurrence. ONC201 is the first clinical bitopic DRD2 antagonist/ClpP agonist and is under evaluation in Phase II trials for gliomas and other cancers. We previously reported in vitro studies suggesting dysregulated dopamine receptor expression and enhanced ONC201 sensitivity among H3 K27M-mutant gliomas. Following these observations, adults with midline H3 K27M-mutant glioma patients were enrolled to a dedicated Phase II clinical trial (NCT03295396), a multi-arm Phase II trial (NCT0252569), and expanded access protocols under the Sponsor's IND. An integrated radiographic analysis with an objective response rate primary endpoint in patients who received ONC201 monotherapy with confirmed H3 K27M-mutant glioma (not primarily in the pons or spinal cord and without leptomeningeal spread) that was progressive and measurable disease by RANO criteria, >90 days from completion of prior radiation, and had KPS >60. As of December 15, 2018, 15 patients have received single agent ONC201 who meet these criteria (n=9 NCT03295396; n=5 NCT0252569; n=1 expanded access). ONC201 was orally administered at 625 mg weekly, except for one patient dosed once every 3 weeks. As midline gliomas can exhibit a mixture of contrast-enhancing and non-contrast-enhancing disease, objective response was assessed by blinded independent central review using RANO-HGG and RANO-LGG criteria for each patient. Best response to date by RANO-HGG criteria is at least 27%: 1 CR, 3 PR, 7 SD, and 4 PD; by RANO-LGG is at least 36%: 1 CR, 1 PR, 3 minor response (MR), 4 SD, 5 PD, 1 unevaluable. By RANO-HGG, median onset of response is 2.6 months (range 1.3–3.4); median duration of response has not been reached with a median follow-up of 7.7 months (range 1.8–29.8). Updated radiographic response, pharmacodynamics, safety, and other clinical outcomes will be reported.

ACTR-35. A STUDY OF RACE AND SOCIOECONOMIC STATUS IMPACTING THERAPEUTIC CLINICAL TRIAL ENROLLMENT IN ADULT GLIOMAS PATIENTS

Ramin Morshed[1], Sheantel Reihl[1], Sofia Kakaizada[1], Eric Zhang[1], Jacob Young[1], Jennifer Clarke[1], Nicholas Butowski[1], Jennie Taylor[2], Nancy Ann Oberheim-Bush[1], Manish Aghi[1], Mitchel Berger[1], Susan Chang[1], and Shawn Hervey-Jumper[3]; [1]University of California, San Francisco, San Francisco, CA, USA, [2]Division of Neuro-Oncology UCSF, San Francisco, CA, USA, [3]Department of Neurological Surgery, University of California, San Francisco, San Francisco, CA, USA

OBJECT: Under-enrollment in clinical trials significantly limits valid analyses of clinical interventions and generalizability of findings. Often it results in premature study termination, with estimates of 22% to 50% of clinical trials terminated due to poor accrual. Currently, there are limited reports addressing the influence of race/ethnicity and socioeconomic status on clinical trial enrollment in patients with adult glioma. The goal of this study was to determine if these factors impact clinical trial participation for glioma patients. METHODS: 852 adult patients were identified from the UCSF Tumor Board Registry and analyzed to determine the rate of therapeutic clinical trial consideration, tumor board recommendation, and study enrollment based on clinical reports in their electronic medical records. RESULTS: At initial diagnosis, 30.7% and 18.0% of glioma patients were recommended and enrolled in a therapeutic clinical trial, respectively. At recurrence, 38.7% and 25.3% of patients were recommended and enrolled in a clinical trial, respectively. Nineteen percent of the study population belonged to a NIH-designated underrepresented minority group; Asian/Pacific-Islander comprising 10.3% overall. On univariate analysis, only in-state location, distance to the hospital, and WHO grade were associated with consideration, recommendation, and enrollment at initial diagnosis and recurrence. Minority status, insurance type, median household income, and percent below poverty were not associated with clinical trial recommendation or enrollment. CONCLUSION: Race and socioeconomic status did not impact clinical trial consideration, tumor board recommendation, or study enrollment. Our results do not support the premise that provider decisions are impacted by biases based on minority or socioeconomic status.

ACTR-37. ASSOCIATION BETWEEN MGMT PROMOTER METHYLATION SCORE AND SURVIVAL IN PATIENTS WITH GLIOBLASTOMA

Carlos Romo[1], Pavan Shah[1], Yuqing Sun[1], Xiaobu Ye[2], and Stuart Grossman[1]; [1]Johns Hopkins University School of Medicine, Baltimore, MD, USA, [2]Johns Hopkins University, Baltimore, USA

BACKGROUND: MGMT promoter methylation is associated with longer survival in patients with high-grade gliomas who receive alkylating therapy. Methylation status is commonly determined by methylation-specific PCR and results are reported in two forms: a dichotomization of "present" or "not present," and as a methylation score (MGMT/beta-actinx1000). The primary objective of this study is to determine the association between the degree of methylation and overall survival (OS) in newly diagnosed patients with glioblastoma. METHODS: A retrospective IRB-approved study was conducted of 684 patients treated at Johns Hopkins from 2007–2015. Adults with a histologically confirmed glioblastoma treated with standard therapy were included in the analysis. OS was estimated from the date of diagnosis to time of death or last follow up using the Kaplan–Meier method. Cox regression model was used to assess possible positive association between MGMT score and OS. For purposes of this analysis IDH1-mutated patients were excluded. RESULTS: In 100 evaluable patients, median age at diagnosis was 56 years [45–77]. Fifty-two patients were MGMT promoter methylated (score ≥2.00) and 48 were unmethylated. The median OS was 31 months in the methylated patients and 15 months in the unmethylated (p=0.0001). Methylated patients had MGMT scores ranging from 2.53-1278. The methylated scores were classified into 3 groups; #1: 0-25th percentile, #2: 25-75th percentiles, and #3: >75th percentile. mOS was: 30.8 months for group 1 (n=13); 34.8 months for group 2 (n=27); and 20.9 months for group 3 (n=12) (p=0.19). Difference in mOS between groups 1 and 3 was not statistically significant (HR 0.819 [95% CI, 0.3–2.2], p=0.69). DISCUSSION: The prognostic value of MGMT promoter methylation in patients with glioblastoma was replicated in our study sample. The degree of methylation reported as a score on routine testing does not appear to be directly related to OS in this patient population.

ACTR-38. A SINGLE CENTER STUDY: LONG-TERM OUTCOMES OF COMBINED CHEMORADIATION THERAPY WITH TEMOZOLOMIDE FOR NEWLY DIAGNOSED GLIOBLASTOMA IN KOREAN PATIENT

Kyeong-O Go[1], Ha Young Yang[2], Kihwan Hwang[1], Jung Ho Han[3], Hyoung Soo Choi[4], Yu Jung Kim[5], Chan Woo Wee[6], In Ah Kim[7], Gheeyoung Choe[8], and Chae-Yong Kim[9]; [1]Department of Neurosurgery, Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [2]Seoul National University College of Medicine, Seoul, Republic of Korea, [3]Seoul National University Bundang Hospital, Seongnam, Kyonggi-do, Republic of Korea, [4]Department of Pediatrics, Seoul National University Bundang Hospital, Seongnam, Kyonggi-do, Republic of Korea, [5]Department of Internal medicine, Seoul National University Bundang Hospital, Seong nam, Kyonggi-do, Republic of Korea, [6]Department of Radiation Oncology, Seoul National University Bundang Hospital, Seongnam, Kyonggi-do, Republic of Korea, [7]Department of Radiation Oncology, SeoulNational University Bundang Hospital, Seongnam, Kyonggi-do, Republic of Korea, [8]Seoul National Univeristy Bundang Hospital, Seoungnam, Republic of Korea, [9]Department of Neurosurgery, Seoul National University Bundang Hospital, Goyang, Republic of Korea

In newly diagnosed glioblastoma (GBM), Temozolomide (TMZ) during and after radiation therapy has become standard treatment. This study describes the long-term use and follow-up results of this therapy for GBM. From 2004 to 2013 in a single institute, 112 Korean patients with newly diagnosed GBM were analyzed retrospectively. The Kaplan-Meier method, the two-sided log-rank test and Cox's regression analysis was used to determine survival and its affecting factors. The toxicities of TMZ were evaluated using CTCAE v5.0. During the median follow-up period of 18.8 months, median PFS and OS were 9.2 and 20.3 months, respectively. This better survival outcome than the Stupp's original study might be probably a large treatment effect of a single institution, ethnicity, and associated genetic factors. The TMZ during radiation therapy was completed in 108 patients (96.4%) and TMZ after radiation therapy in 59 patients (52.7%). Eight patients presented with grade 3 or 4 hematologic toxic effects during the protocol. Sixty-six patients (58.9%) received salvage treatment because of the poor response to adjuvant treatment or progression of the disease who achieved completion of adjuvant treatment was shown significantly longer median OS (p= 0.007) and PFS (p< 0.001). Age (< 60 years), preoperative KPS score (≥ 90), the extent of resection (≥ 78% by volumetric measurement, gross total resection), and completion of the Stupp's protocol were significant factors affecting better survival. Between the sexes, and ages over 65 years did not show any significant difference among their groups. With marginal significances, the mutated IDH-1 and the methylated MGMT promoter showed longer median PFS(p= 0.075 and 0.777, respectively) and OS (p= 0.085 and 0.131, respectively). TMZ during and after radiation therapy might be effective and safe for newly diagnosed Korean patients with GBM. Further studies about various clinical and genetic factors affecting better survival are mandatory.

ACTR-39. PAMIPARIB IN COMBINATION WITH RADIATION THERAPY (RT) AND/OR TEMOZOLOMIDE (TMZ) IN PATIENTS WITH NEWLY DIAGNOSED OR RECURRENT/REFRACTORY (R/R) GLIOBLASTOMA (GBM); PHASE 1B/2 STUDY UPDATE

Anna Piotrowski[1], Vinay Puduvalli[2], Patrick Wen[3], Jian Campian[4], Howard Colman[5], Michael Pearlman[6],