incidence of seizures in glioblastoma (GBM) patients has been reported to be between 40% and 60%, and most patients with GBM receive some antiepileptic drugs (AEDs) in the perioperative and postoperative periods. Research in this area has focused on various AEDs and their anticonvulsant efficacy of AEDs; however, most of them are retrospective studies and the results are inconsistent. Here, we carried out an observational study to evaluate the impact of AEDs on overall survival (OS) in GBM patients who received temozolomide for postoperative adjuvant chemotherapy. Methods: Data of 190 patients with newly diagnosed GBM, treated at Kobe University in the period between January 2007 and January 2016, were retrospectively analyzed. Prognostic influence of enzyme-inducing AEDs (EIAEDs), non-EIAEDs, levetiracetam (LEV), and avoidant AEDs on survival were analyzed by Kaplan-Meier method. Further, a Cox regression analysis was performed to evaluate the association between potential prognostic factors [age, preoperative KPS, extent of tumor resection, MGMT promoter methylation status, and AED (EIAEDs, non-EIAEDs, none)] and progression-free survival (PFS) or OS. Results: There was no significance between the median OS for patients who received EIAEDs (median, 16.3 months; 95% confidence interval [CI], 14.0-24.5 months) and that for patients who received non-EIAEDs (median, 17.9 months; 95% CI, 17.8-20.5 months). Also, no association with longer OS was observed for LEV use at the end of initial chemoradiotherapy. There was no significant difference of OS and PFS between the patients with AEDs and those without AEDs. In the multivariate analysis, MGMT promoter methylation status and the extent of removal were associated with longer OS and PFS. OS and PFS were correlated with the results of the multivariate analysis. The results indicated no association between OS and non-EIAEDs use. Although not statistically significant, administration of some AEDs may provide a favorable prognosis in patients with GBM.

NCMP-12. Glioma-Related Epilepsy: Clinical and Pathological Correlates
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INTRODUCTION: The overall incidence of brain tumor-related epilepsy among all causes of epilepsies ranges from 4-9%. Epileptic seizures are associated with brain tumor in approximately 30-50% of patients. Glioma is the most common cause of primary brain tumors, contributing nearly 50% of all cases. In high grade glioma seizure frequency is 20-50%, but in low grade it can be up to 90%. There have been multiple publications describing epilepsy frequency in low grade and high grade glioma but few have described the relationship between seizures and IDH1 R132H mutation. Here we report the relationship between seizures and IDH1 R132H mutation.
METHOIDS: This is an observational retrospective clinical study. Medical records and neuromaging data were reviewed for all newly diagnosed patients with brain tumor and pathology consisting of oligodendroglioma and astrocytoma WHO grade II and III at the Montreal Neurological Institute and Hospital between 2011 and 2015. IDH1 R132H status was obtained in all tumors and 1p/19q co-deletion was analyzed in all oligodendrogliomas. The details about related seizures were collected, including seizure semiology, timing in relation to surgery, frequency, and antiepileptic medications used. Tumor location was determined by preoperative MRI. RESULTS: There were a total of 153 subjects included in the study. Preoperative seizure frequency was 66% (n=103). There was no association between single or multi-focal location of tumor and preoperative seizure frequency (n=103, p=0.186). Tumors with mutated IDH1 had a higher rate of preoperative seizure at presentation (74%, n=62 vs 49%, n=37, p=0.007). Seizure freedom at 1 year was increased by gross total resection compared to subtotal resection or biopsy (90%, n=20 vs 67%, n=53, p=0.049). CONCLUSION: Presence of an IDH1 mutation, but not tumor location, is associated with higher risk of pre-operative seizure in low and intermediate grade gliomas. Extent of surgical resection may influence seizure control at 1 year in patients with low and intermediate grade gliomas.
NEURO-COGNITIVE OUTCOMES
NCOG-01. Patient-Reported Cognitive Concerns and Quality of Life in Brain Metastases
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BACKGROUND: While treatment options for brain metastases continue to evolve, prognosis remains poor for morbidity and survival. Quality of life (QOL) is increasingly emphasized and assessed via patient-reported outcomes. Although studies show most patients are cognitively impaired on neuropsychological testing, few have evaluated patients' subjective cognitive concerns and QOL in relation to other aspects of QOL. METHODS: A cross-sectional sample of brain metastasis patients completed measures assessing subjective cognitive function in multiple domains as well as functional limitations, illness intrusiveness (i.e., interference in valued activities and relationships), existential distress, anxiety and depression. RESULTS: Seventy percent completed the survey; 40% were treated with SRS alone, 19% with WBRT+SRS, 7% with surgery and/or focal radiotherapy only, and 34% had not received CNS-directed therapy. Patients ranged in age from 31-87, 64% were female. Prevalence of self-reported cognitive dysfunction was 32% with attention and processing speed most common (19% of patients each), followed by executive, memory and language functions (14, 11 and 9%). These cognitive concerns did not relate to patients’ age or differ by sex, but were associated with symptoms of anxiety (r’s = 0.385 to 0.352, p’s < .003), depression (r’s = 0.508 to 0.650, p’s < .001), existential distress (r’s = 0.338 to 0.341, p’s < .01) and illness intrusiveness (r’s = 0.333 to 0.442, p’s < .05). Processing speed and attentional deficits were additionally linked to limitations in instrumental activities of daily living (r’s = 0.262 and 0.272, p’s < .05). Patient who had undergone surgery and/or focal radiotherapy reported greater cognitive impairment than other CNS treatment groups. DISCUSSION: Results show a significant association between brain metastasis patients’ subjective cognitive concerns and QOL in the effect of CNS treatment on patient-reported cognitive outcomes. These data may be used to develop supportive care initiatives for brain metastasis patients.
Abstracts

radiosensitivity. Less decline/improvement in HVLT following HA-WBRT for patients with higher pre-treatment intracranial metastatic burden supports the importance of WBRT-induced intracranial control on cognition. These imaging biomarkers for cognitive toxicity will be further explored on NRG CC001 and CC003, phase III trials of WBRT with or without HA, Supporting NCI grants: U10CA180868, U10CA180822, U24CA180803, UG1CA189867.

NCOG-03. PERSONALITY TRAITS IN PATIENTS WITH NEUROEPITHELIAL TUMORS – A PROSPECTIVE STUDY

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Aim of this study was to analyze personality traits in patients with neuroepithelial brain tumors. Personality alteration is a common feature in brain tumors which is known about associations between specific personality changes and brain tumors. We assessed potential factors influencing personality such as tumor location, tumor grade and tumor volume and compared them with neuropsychological tests. 73 patients with intrinsic brain tumors and two in the followup were acquired were acquired. Data were acquired pre- and postoperatively and 3 and 9 months postoperatively. The following tests were acquired: Mini-Mental State examination (MMSE), short form health survey (SF-36), Beck’s Depression Inventory II (BDI-II), and the NEO Five-Factor Inventory (NEO-FFI) for the five factors of personality (openness, agreeableness, neuroticism, extraversion, and conscientiousness). Patients with intrinsic brain tumors showed lower scores regarding the factor openness and a decrease of conscientiousness over time compared to the normal population. No significant influencing factors (tumor entity, location) were found regarding personality traits; just a slight correlation between tumor volume and the factor openness was observed. Compared to the normal population, brain tumor patients had higher scores of BDI-II, with a significant preference for women and KPS. Neurotism was associated with depression and lower mental health, whereas conscientiousness and neuroticism showed no association with depression. Patients with brain tumors have differences in personality traits compared to the control population, with an emphasis on the factor openness. No significant confounding factors like tumor grade, entity, or location were found for personality traits.

NCOG-04. ANALYSIS OF EXAMINER ERRORS ON COGNITIVE TESTING IN MULTI-SITE STUDIES

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This is a growing interest in cognitive function as an outcome measure in brain tumor clinical trials. A 3-test battery has been recommended, including the Trail Making Test, Parts A and B (TMT A and TMT B), the Hopkins Verbal Learning Test-Revised (HVLT-R), and the Controlled Oral Word Association Test (COWAT). Use of this battery allows direct comparison and pooling of data across studies. We have used this battery with clinical outcomes (e.g., Brown et al 2016). By necessity, psychometric examiners must be trained at many sites for multi-site studies, and some examiner error in testing and recording results is inevitable. To manage this, we re-score all cognitive test protocols for our studies prior to data entry. However, there is a growing interest in on-site data entry as an efficiency measure. We looked at error rates in cognitive testing using the aforementioned 3-test battery and standard training of examiners to inform quality-improvement measures and assess whether on-site entry would be prudent. In 300 consecutive exams, we found that 189 (37.8%) had at least one error. Of 274 total errors, 29 were not correctable upon review, leading to invalidation (1.3% of 2,277 tests administered). 48.5% of the errors would not have been detected with basic electronic on-site entry. Error rates (at least one or more errors/times given) for each test were TMT A 6%, TMT B 9%, COWAT 21.2%, HVLT-R Learning 7.5%, HVLT-R Delayed Recall 7.1% and HVLT-R Recognition 11.6%. The majority of the invalidating errors 262/29 (89.7%) were on the Trail Making Test. CONCLUSION: Examiner errors are common in multi-site studies, but most are correctable upon review. We will discuss these results as well as the types of errors that might occur that cannot be detected, how these results should inform test selection and examiner training, and implications for on-site data entry.

NCOG-05. TIME TO FUNCTIONAL AND COGNITIVE DECLINE IN A PHASE 3 TRIAL OF TUMOR TREATING FIELDS WITH TEMOZOLOMIDE VERSUS TEMOZOLOMIDE ALONE IN PATIENTS WITH NEWLY DIAGNOSED Glioblastoma

Garth A Nicholas1, Holger Hirtz2, Jacob Eassaw3, Thierry Muanza3, Sandra Bahary4, Constantinos Hadjipanayis5, James Urbanic5, 6, Deepak Khuntia1, Yolanda Garces3, Caterina Giannini1, David Roberge1, Karla Ballman1, Jane Cerhan1, S. Keith Anderson1, Xiaoxia Carrero3, Anthony Whitton4, Jeffrey N Greenspoon4, Ian Partridge5, Nadia N. Laack2, Jonathan American Brain Tumor Association Test (COWAT). Use of this battery allows direct comparison and pooling of data across studies. We have used this battery with robust outcomes such as long term survival and overall survival of patients with newly diagnosed glioblastoma who had not progressed during their initial radiation therapy with TMZ. Time dependent differences in patients’ performance status and cognitive capabilities were protocol prespecified analyses. Time to deterioration (TTD) in performance status was measured using the Kaplan-Meier method considering a sustained decrease in Karnofsky performance score (KPS) of ≤20 points or death within 90 days of the last follow up event. Patients without decline in KPS were censored at their last evaluation. TTD in cognitive function was measured using the Kaplan-Meier method considering a sustained decrease in Mini-Mental Status Score (MMSE) of ≤20 points or death within 90 days of the last evaluation of an event. Patients with a decline in MMSE of ≤20 points were censored at their last evaluation. TTD in KPS was similar to time to radiologic disease progression and was significantly longer in patients treated with TTFields/TMZ than with TMZ alone (median 5.5 months vs 3.9 months; HR 0.84; p=0.0092). TTD in MMSE was longer than time to deterioration in KPS in both arms, and was significantly longer in patients treated with TTFields/TMZ vs. TMZ alone 16.7 months vs 13.0 months; HR 0.74; p=0.012). Patients with compliance ≥75% with TTFields had significantly longer TTD in MMSE (p=0.0028) but not in KPS (p=0.652) compared to patients with compliance <75%. These results suggest that decline in performance status and cognitive capabilities are correlated with disease progression and extended by the addition of TTFields to TMZ.

Glioblastoma is a disease characterized by progressive decline in patients’ functional status and cognitive abilities. The EF-14 phase 3 trial demonstrated that adding TTFields to temozolomide (TTFields/TMZ) compared to temozolomide alone (TMZ) led to a significant increase in overall survival and overall survival of patients with newly diagnosed glioblastoma who had not progressed during their initial radiation therapy with TMZ. Time dependent differences in patients’ performance status and cognitive capabilities were protocol prespecified analyses. Time to deterioration (TTD) in performance status was measured using the Kaplan-Meier method considering a sustained decrease in Karnofsky performance score (KPS) of ≤20 points or death within 90 days of the last follow up event. Patients without decline in KPS were censored at their last evaluation. TTD in cognitive function was measured using the Kaplan-Meier method considering a sustained decrease in Mini-Mental Status Score (MMSE) of ≤20 points or death within 90 days of the last evaluation of an event. Patients with a decline in MMSE of ≤20 points were censored at their last evaluation. TTD in KPS was similar to time to radiologic disease progression and was significantly longer in patients treated with TTFields/TMZ than with TMZ alone (median 5.5 months vs 3.9 months; HR 0.84; p=0.0092). TTD in MMSE was longer than time to deterioration in KPS in both arms, and was significantly longer in patients treated with TTFields/TMZ vs. TMZ alone 16.7 months vs 13.0 months; HR 0.74; p=0.012). Patients with compliance ≥75% with TTFields had significantly longer TTD in MMSE (p=0.0028) but not in KPS (p=0.652) compared to patients with compliance <75%. These results suggest that decline in performance status and cognitive capabilities are correlated with disease progression and extended by the addition of TTFields to TMZ.

BACKGROUND: It has been our recent finding that, when substituted for whole brain radiotherapy (WBRT) as an adjuvant to resection of a brain metastasis, radiosurgery (SRS) results in improved cognitive outcomes and equivalent overall survival — this despite inferior long-term local control. A subgroup of patients will be long-term survivors following local treatment of their brain metastases. Here we report an unplanned analysis of the outcomes of patients surviving more than 12 months following surgery. METHODS: Patients were randomized to either radiosurgery or WBRT after resection of a brain metastasis. The primary endpoints were neurocognitive progression and overall survival. In this report, cognitive deterioration is defined as a 1-SD drop in at least 1 cognitive test. This study is registered with ClinicalTrials.gov, number NCT01372774. RESULTS: Between July 2011 and December 2015, 194 patients were enrolled with a median follow-up of 11.1 months (maximum 82 months). Basic demographics and neurological outcomes were well-balanced between study arms. At 12 months, there were 47 patients alive in the SRS arm and 42 in the WBRT arm; at 24 months, there were 14 and 22 survivors in the SRS and WBRT arms, respectively. At 12 months the intracranial control was 72% in the WBRT arm and 34% in the SRS arm (p=0.0001). At 12 months, 60% of SRS patients tested had neurocognitive progression vs. 91% of WBRT-treated patients (p=0.02). At 24 months, 40% of SRS patients tested had neurocognitive progression vs. 75% of WBRT-treated patients (p=0.03). At 24 months, no radiosurgery patient had a significant decline in immediate recall (HVLT-R) vs. 50% of WBRT patients (p=0.015). CONCLUSIONS: Decline in cognitive function occurs early after treatment of brain metastases and remains relatively stable over time. Despite inferior intracranial control, the cognitive advantage of SRS is preserved in long-term survivors. SUPPORTED BY US01CA108821, U01 CA040882, U10CA180868, UG1CA189823.