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NCOG-21. INTERIM RESULTS OF THREE COGNITIVE REHABILITATION STRATEGIES IN PATIENTS WITH LOWER GRADE GLIOMAS

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overall survival was 9.4 months (95% CI: 7.8-12.2). Variables associated with worse survival included longer length of stay (HR: 1.15, 95% CI: 1.02-1.30,  $p = 0.02$ ), discharge destination other than home (HR: 1.91, 95% CI: 1.01-3.6,  $p = 0.04$ ), and any postop complication (HR: 3.7, 95% CI: 1.87-7.3,  $p < 0.001$ ). The presence of any or multiple medical comorbidities was not associated with worse survival ( $p = 0.93$  and  $0.19$ , respectively). **CONCLUSIONS:** The presence of medical comorbidities is not associated with worse survival in elderly patients undergoing surgery for GBM. In order to maximize survival in these patients, avoidance of postoperative complications is paramount, along with a short hospital stay and attempt to discharge these patients to their home.

#### NCOG-18. IS THE RANO CRITERIA FOR LOW-GRADE GLIOMA RELIABLE IN THE CLINICAL SETTING? – A RELIABILITY STUDY

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**INTRODUCTION:** Magnetic resonance imaging (MRI) is a fundamental component of longitudinal neuro-oncology evaluation and decision-making. The Response Assessment in Neuro-Oncology criteria for low-grade gliomas (RANO<sub>LGG</sub>) was designed as an outcome measure for clinical trials. Thus, this project intends to study the reliability of RANO<sub>LGG</sub> in the clinic setting. **METHODS:** 21 pairs of brain MRIs, that averaged three years apart, were selected from 21 patients with tissue diagnosis of WHO grade 2 gliomas. Two neuro-oncologists and two neuro-radiologists reviewed and independently scored the MRI pairs according to RANO<sub>LGG</sub> categories of progressive disease, stable disease, minor response, partial response, and complete response. Kappa-Fleiss (KF) was used to evaluate agreement among reviewers. **RESULTS:** Reviewers awarded identical scores in only 33% of MRI pairs and there was a complete disagreement in one MRI pair. Overall reliability of the criteria in the clinical setting is moderate (KF = 0.44). Agreement between neuroradiologists (KF = 0.51) and between neuro-oncologists (KF = 0.48) were similar. Interpretation of post-contrast T1-weighted images had a better agreement (KF = 0.31) than T2/FLAIR-weighted images which had a poor agreement (KF = -0.02). Classification of progression versus non-progression had only a moderate agreement (KF = 0.49). History of radiation therapy or chemotherapy did not influence the criteria reliability (fisher exact text,  $p = 0.58$ ,  $p = 0.27$ , respectively). **CONCLUSION:** RANO<sub>LGG</sub> reliability in the clinical setting is moderate, therefore it should be used cautiously for clinical decision-making. Other tools that can support the neuro-oncologist in the follow-up of patients with low-grade glioma are additional MRI sequences other than T2/FLAIR and contrast – weighted images, computer-aided diagnosis such as volumetrics, spectroscopy, positron emission tomography, and multidisciplinary tumor boards. Likewise, when image criteria for low-grade gliomas are designed, T2/FLAIR should be used guardedly, due to low interpretation agreement.

#### NCOG-19. BEVACIZUMAB IN REAL LIFE PATIENTS WITH RECURRENT GLIOBLASTOMA: BENEFIT OR FUTILITY?

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Angiogenesis represents a hallmark of glioblastoma but most trials disappointed and failed to change the poor outcome of this disease. However, Bevacizumab (Bev) is widely used in clinical practice by expert oncologists due to experience or efficacy in real life. We retrospectively reviewed the use of Bev and its benefit in terms of Time to treatment failure (TTF), Overall Survival (OS), Objective Response Rate (ORR) and clinical benefit. **METHODS:** We analyzed two hundred and two patients treated at Gustave Roussy Cancer Campus with Bev until definitive failure for recurrent glioblastoma between 2006 and 2016. Patients were treated with Bev alone or in association with radiotherapy, temozolomide, lomustine or irinotecan. **RESULTS:** The median duration of Bev treatment until definitive failure was 6 months. The median TTF was 7.27 months (95% CI 6.30-8.24) and the median OS from diagnosis was 22.43 months (95% CI 19.68-25.18). Two patients were still alive without active treatment at the end of study. A hundred and fourteen (56%) patients experienced symptom amelioration and seventy-five (37%) improved their Performance Status. Fifty percent of patients exhibited Partial and Complete Response on MRI, as best radiological response, within 1.6 months. No patient had anaphylactic reaction. Grade 1-2 hypertension (HT) (17%) and grade 1 (10%) proteinuria were most common. Six patients presented lethal toxicity: 4 with GI perforation, 1 p with cerebral hemorrhage and 1 p with arterial bleeding. HT was correlated with treatment response in 67% of patients. A neutrophil count superior to 6000/mm<sup>3</sup> was associated with longer TTF (mTTF 8.23m (95% CI 6.64-

9.82). **CONCLUSION:** This retrospective study reports a substantial clinical benefit of Bev in patients with recurrent glioblastoma with an acceptable toxicity profile. As the panel of therapeutic option is still very limited in these tumors, this work supports the maintained use of Bev as a therapeutic option.

#### NCOG-20. AWAKE SURGERY FOR RIGHT FRONTAL LOBE GLIOMA CAN IMPROVE THE RESECTION RATE AND PRESERVE HIGHER COGNITIVE FUNCTIONS

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**OBJECTIVE:** Awake surgery is the standard treatment to preserve motor and language functions. The aim of this study is to evaluate the awake surgery for the patients with right frontal lobe (RFL) glioma on resection rate and preservation of higher cognitive functions. **METHODS:** Out of the 139 cases that underwent awake surgery at our hospital between 2013 and 2019, 34 cases (mean age: 47.8 years) of RFL glioma were included in this study. The WHO classification was grade II, III, and IV for 15, 13, and 6 cases, respectively. We evaluated visual spatial cognition (VSC), spatial working memory (SWM), and social cognition (SC) before and after the surgery. These relevant areas were mapped intraoperatively. We did not map these areas in the cases in which the task could not be accomplished. Therefore, each function was divided into an intraoperative evaluation group (EG) and a non-evaluation group (NEG), and the resection rate and functional outcomes were compared. **RESULTS:** The removal rate was significantly higher in the EG group for VSC and SC than that in the NEG ( $p = 0.0078$  and  $0.0024$ , respectively). The chronic disability rate of VSC was significantly lower in the EG than that in the NEG (5.6% vs. 31.3%,  $p = 0.043$ ). None of the patients had postoperative disability of SWM in the EG which is significantly lower than that in the NEG (16.7%,  $p = 0.049$ ). SC tended to have a lower disability rate (20.0%) in the EG compared to that in the NEG (45.8%). The probability that the posterior deep part of the middle frontal gyrus, which is the relevant area of VSC, was resected higher in the NEG ( $p = 0.0052$ ). **CONCLUSIONS:** We scientifically verified that the awake surgery for RFL glioma contributes to the improvement of resection rate and the preservation of higher cognitive functions.

#### NCOG-21. INTERIM RESULTS OF THREE COGNITIVE REHABILITATION STRATEGIES IN PATIENTS WITH LOWER GRADE GLIOMAS

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**BACKGROUND:** Patients with lower grade (2 and 3) gliomas (LrGG) are living longer, but often with cognitive impairments from their tumor and treatments. However, cognitive assessments and access to cognitive rehabilitation are not a standard part of care. We present preliminary results of a pilot study investigating feasibility and efficacy of three cognitive rehabilitation strategies for stable LrGG patients – in-person manualized cognitive rehabilitation; iPad based cognitive rehabilitation program of retraining and compensation strategies (ReMind); or daily instructional text messages (Healthy SMS). **METHODS:** Eligible patients were adults with clinically and radiologically stable LrGG, > 6 months from last treatment, and  $\geq 1$  standard deviation (SD) below normal on  $\geq 2$  domains of neuropsychological assessments. Patients were first offered in-person cognitive rehabilitation or randomized to ReMind or Healthy SMS if unable to attend in-person. Interventions lasted 3 months. Neuropsychological and HRQOL assessments, using PROMIS NeuroQOL, were conducted at baseline, 3, and 6 months post-intervention. Feasibility was defined as attending  $\geq 80\%$  of in-person sessions; completing  $\geq 80\%$  of ReMind tasks; or not opting out of Healthy SMS texts. **RESULTS:** To date 23/60 patients have enrolled: 11 in-person and 12 randomized to ReMind (5) or Healthy SMS (7). Demographic and clinical characteristics were similar between cohorts. Median age at testing was 46 years, with 65% female, and 78% having received prior radiation (median 4.1 years, range 3.2 – 11.5). At baseline, processing speed was the most common domain of impairment with 43%  $\geq 1.5$  SD below normal and 36% patients reporting subjective cognitive impairment on HROQL assessment. Feasibility was 71% for in-person rehabilitation; 50% for ReMind; and 100% for Health SMS. **CONCLUSION:** These pre-

liminary results demonstrate that stable LrGG patients with subjective and objective cognitive impairments can reasonably engage in cognitive rehabilitation interventions. Updated data including post-intervention neuropsychological and HROQL related changes will be presented.

#### NCOG-23. PATTERNS OF DISTRESS IN OLDER PATIENTS WITH GLIOBLASTOMA: A FOLLOW-UP TO A SINGLE INSTITUTION CROSS-SECTIONAL STUDY OF DISTRESS IN PRIMARY BRAIN TUMOR PATIENTS

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**INTRODUCTION:** We previously reported to SNO, high levels of psychosocial distress in adult patients with primary brain tumors (PBTs), particularly during the first 6 months following diagnosis. The purpose of this follow-up study was to identify patterns of distress among older ( $\geq 65$  years) patients with glioblastoma (GBM) compared to their younger (ages 18-64) counterparts. **METHODS:** In our initial cross-sectional study, we collected the National Comprehensive Cancer Network's Distress Thermometer (NCCN-DT) and problem list from adult patients with PBTs (WHO grades I-IV) seen at our institution between December 2013 and February 2016. We performed subsequent analyses on a subset of patients with GBM. **RESULTS:** We identified 343 patients with GBM from the original dataset, of which 23.0% (n = 78) were  $\geq 65$  years old. The proportion of patients  $\geq 65$  years old with elevated distress (i.e. DT  $\geq 4$ ) was greater than the proportion of younger patients reporting elevated distress (47.4% vs 30.6%;  $p = 0.0068$ ). Elevated distress was significantly greater during the first 6 months post diagnosis for all ages ( $p = 0.008$ ). In subgroup analyses, a decrease in distress beyond 6 months was seen in younger patients (45.7% vs 27.4%;  $p = 0.021$ ), but not in older patients. In older patients, a greater number of problems were selected on the NCCN DT and problem list tool: emotional and physical concerns were reported more frequently compared to their younger counterparts. Older patients were more likely to report difficulty with "bathing" and "getting around" ( $p = 0.009$ ,  $p < 0.001$ , respectively). There were no differences in older versus younger GBM patients with regard to housing, transportation, treatment decisions, depression, fatigue, or memory. **CONCLUSIONS:** In contrast to their younger counterparts, older patients with GBM experienced elevated levels of distress and a greater absolute number of specific psychosocial problems, mostly related to emotional and physical concerns.

#### NCOG-24. WAKE FOREST NCORP RESEARCH BASE FEASIBILITY STUDY OF RAMIPRIL FOR PREVENTING COGNITIVE DECLINE IN GLIOBLASTOMA PATIENTS RECEIVING BRAIN RADIOTHERAPY (WF-1801)

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**INTRODUCTION:** Chronic neuro-inflammation after brain radiotherapy (RT) contributes to radiation-induced cognitive decline (RICD). The renin angiotensin system (RAS) may mediate this inflammatory cascade after RT. Ramipril is an angiotensin-converting enzyme inhibitor used to treat hypertension and has good blood-brain barrier penetration. By blocking RAS activation, ramipril reduces neuro-inflammation and preclinical data show that ramipril administration during RT can prevent RICD. **METHODS:** WF-1801 is an ongoing feasibility study that will enroll a total of 75 patients. Patients  $\geq 18$  with newly diagnosed and pathologically confirmed GBM who will receive chemoradiation are eligible. All participants take ramipril daily during RT and for 4 months thereafter. Ramipril is titrated from 1.25mg to 5mg daily over 3 weeks. A cognitive battery that includes the Hopkins Verbal Learning Test-Revised (HVLT-R), Trail Making Test (TMT), and Controlled Oral Word Association test (COWA) is administered at baseline, end of RT, and 1-month and 4-months post-RT. The co-primary endpoints are retention rate (with retention defined as compliance with  $> 75\%$  of drug therapy doses) and neurocognitive function at 1-month post-RT. To estimate the effect of ramipril on cognitive function, performance on the cognitive battery will be compared to a historical control (cognitive data from the control arm of RTOG 0825). ApoE genotyping is being performed as a correlative study. **RESULTS:** 31 of a planned 75 participants have been enrolled over 14 months. 20 of 31 (64.5%) are male. 21 (67.7%) are between the age of 40-64. 20 (95.6%) are white and 29 (93.6%) are not Hispanic or Latino. **CONCLUSION:** Despite a pause in accrual due to COVID-19, we are easily meeting planned accrual goals. Community oncology-based clinical trials of interventions to prevent cognitive toxicity appear to be feasible. GBM patients seem eager to enroll in studies seeking to prevent cognitive decline. Supported by NCI grant UG1CA189824.

#### NCOG-25. EFFICACY OF ANTICONVULSANT THERAPY IN GLIOMA PATIENTS

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Gliomas account for 30% of primary brain tumors and can frequently present with seizures. There are few guidelines for usage of anticonvulsant therapy in glioma patients. Some clinicians utilize anticonvulsant therapy in all glioma patients as a means of prophylaxis, whereas other clinicians prescribe anticonvulsant therapy only in patients that experience seizures. In this single-institution retrospective cohort study, we evaluate the effect of commonly prescribed anticonvulsant levetiracetam on incidence of post-operative seizures and overall survival in primary glioma patients. 436 patients met the inclusion criteria for this study. 35% of patients presented with a pre-operative seizure and 63% of patients received pre-operative Levetiracetam. The incidence of a seizure within 1 year of tumor resection was 31%. On multivariate logistic regression analysis of patient pre-operative clinical and imaging characteristics, it was found that only a pre-operative seizure ( $p = 0.02$ ) significantly increased the odds of a post-operative seizure within 1 year of tumor resection. Neither pre-operative levetiracetam ( $p = 0.31$ ), intra-operative levetiracetam ( $p = 0.59$ ), or post-operative levetiracetam ( $p = 0.75$ ) significantly reduced the odds of a post-operative seizure. Using a cox proportional hazards model, pre-operative levetiracetam ( $p = 0.11$ ), intra-operative levetiracetam ( $p = 0.34$ ), and post-operative levetiracetam ( $p = 0.88$ ) do not significantly affect overall survival. Our findings reveal that glioma patients are often prescribed anticonvulsant medication regardless of whether they have had a pre-operative seizure. Most patients also receive anti-convulsant medication in the peri-operative and post-operative setting regardless of whether they have had pre-operative or immediate post-operative seizures. Use of pre-operative or intra-operative levetiracetam as a prophylactic measure does not impact the incidence of post-operative seizures. Furthermore, anti-convulsant therapies do not demonstrate a survival benefit in our study. These results provide a rationale for re-evaluating the use of anti-convulsant medications in glioma patients that do not have seizure symptoms.

#### NCOG-26. IMPACT OF GENDER ON TUMOR TREATING FIELDS COMPLIANCE IN PATIENTS WITH GLIOBLASTOMA

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**BACKGROUND:** Tumor treating fields (TTFields) has emerged as a novel antimitotic modality to treat glioblastoma (GBM). Recently, a positive association was reported between TTFields dose at the tumor bed and survival outcomes in GBM patients. Dose density depends upon power density and compliance rate (cumulative amount of time TTFields therapy is delivered to the patient). Increased compliance with TTFields has been proposed as an independent prognostic factor for improved clinical benefits. There is evidence that females tend to respond better than males to standard therapy. However, the impact of gender and age on TTFields compliance is not fully understood in GBM patients. **OBJECTIVE:** To investigate potential interactions amongst age, gender and TTFields compliance in GBM patients. **METHODS:** A cohort of 16 patients (males = 9; females = 7; mean-age = 60.8  $\pm$  7.6 years) with newly diagnosed and recurrent GBM receiving TTFields were analyzed retrospectively. Device usage time was collected from internal log files in each case. The mean duration of TTFields therapy in patients was 4 months. Chi-square and independent sample T-tests were performed to evaluate differences in compliance rates based on patient age and gender and to examine gender-age relationships. Additionally, Pearson correlation analyses were performed to determine associations between gender and compliance rates. The probability (p) value of 0.05 was considered significant. **RESULTS:** A trend ( $p = 0.067$ ) towards greater TTFields compliance was observed in females (80.1  $\pm$  0.11%) versus males (63.0  $\pm$  0.22%). Additionally, there was a strong positive correlation ( $R = 0.73$ ;  $p = 0.058$ ) between age and compliance rates for female patients. There were 6 patients  $\geq 65$  years and 10 patients  $< 65$  years. However, we did not find significant differences in compliance rate and gender variables between patients  $\geq 65$  years and  $< 65$  years of age. **CONCLUSIONS:** Our results demonstrate gender influences TTFields compliance amongst GBM patients. However, future studies with larger cohorts are warranted to validate these findings.

#### NCOG-27. INCREASED OVERALL SURVIVAL AMONG RACIAL MINORITIES AND SUBOPTIMAL USE OF STANDARD OF CARE TREATMENT IN GLIOBLASTOMA MULTIFORME

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