tus. RESULTS: We found that ADAMTSL4 was enriched in GBM, IDH wild-type and MGMT methylated groups. According to the TCGA classification scheme, ADAMTSL4 can act as a potential marker for malignant subtypes. Bioinformatical analyses revealed that ADAMTSL4 was significantly correlated to the immune processes in GBM, especially representing the infiltration of immune cells and complicated tumor microenvironment. Clinically, high expression of ADAMTSL4 was an independent indicator of poorer prognosis. CONCLUSION: The expression of ADAMTSL4 is closely related to the clinicopathologic characteristics of pGBM. Meanwhile, it plays a significantly predictive role in immune processes. For its characteristic of secreted glycoprotein, ADAMTSL4 is a promising circulating biomarker for pGBM, deserving further investigation.

PATH-61. A NOVEL ANALYSIS MODEL OF MGMT METHYLATION PYROSEQUENCING OFFERS AN OPTIMAL PREDICTIVE PERFORMANCE IN GLIOMAS

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The *MGMT* methylation is crucial for clinical decision-making in gliomas. *MGMT* pyrosequencing results were often dichotomized based on a threshold value for the average methylation of several tested CpGs. However, the frequent 'gray zone' results of this method immersed physician in a dilemma, and a novel analysis model which could address this issue is urgently required. In this study, we confirmed the *MGMT* promoter CpGs heterogeneity in 213 high-grade gliomas from two experimental cohorts, which included the seven-site cohort and the eight-site cohort with CpGs 72–78 and CpGs 75–82 tested, respectively. The optimal cut-off value of the methylation status for different CpGs also varied from 4% to 16%. Thus, we raised a novel analysis model, which comprehensively considered each individual CpGs methylation status with its own cut-off value determined by ROC, and the novel analysis defined MGMT promoter methylation when ≥ 3 CpGs exceeded their respective optimal cut-off values. Then we evaluated the predictive accuracy of the novel analysis model in 135 patients received temozolomide from the two experiment cohorts. The results were also validated in an independent cohort including 65 patients, and further compared with the methylation-specific PCR (MSP) approach. In all three cohorts, the novel analysis for CpGs 75–78 accurately predicted the therapeutic prognosis of patients whose methylation levels in the 'gray zone', and improved the AUCs from (0.67, 0.76, and 0.67) to (0.70, 0.84, and 0.72), respectively. Moreover, the advantages of the novel analysis were demonstrated regardless of WHO grades and IDH status. The novel analysis was superior to MSP testing in the validation cohort. Taken together, the novel analysis model offers an optimal clinical predictive performance of *MGMT* pyrosequencing results, and it is suitable for clinical practice in gliomas.

NEURO-COGNITIVE OUTCOMES

NCOG-01. PRESERVATION OF NEUROCOGNITIVE FUNCTION (NCF) WITH HIPPOCAMPAL AVOIDANCE DURING WHOLE-BRAIN RADIOTHERAPY (WBRT) FOR BRAIN METASTASES: PRELIMINARY RESULTS OF PHASE III TRIAL NRG ONCOLOGY CC001

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PURPOSE: NRG CC001, a phase III trial of WBRT plus memantine with or without hippocampal avoidance, sought to evaluate the neuro-protective effects of avoiding the hippocampus using intensity-modulated radiotherapy. METHODS: Adult patients with brain metastases were stratified by RPA class and receipt of prior radiosurgery/surgery and randomized to WBRT+memantine (WBRT+M) versus hippocampal-avoidant WBRT+memantine (HA-WBRT+M) (30Gy in 10 fractions). Standardized NCF tests were performed at baseline, 2, 4, 6, and 12 months. The primary endpoint was time to NCF failure, defined as decline on at least one of the following tests using the reliable change index: Hopkins Verbal Learning Test-Revised, Trail Making Test, or Controlled Oral Word Association. Cumulative incidence was used to estimate time to NCF failure (death without NCF failure was treated as competing risk) with between-arms differences tested using Grays test. To detect an 11% absolute reduction in 6-month NCF failure, 382 analyzable patients were required for 90% power with two-sided =0.05. Due to possible non-compliance, the sample size was increased by 25% (510 patients). RESULTS: From July 2016 to March 2018, 518 patients were randomized. Median age was 61.5 years. Median follow-up for alive patients was 6.1 months. Treatment arms did not differ in grade3 toxicity, overall survival, intracranial progression, or baseline NCF. Time to NCF failure was significantly longer in favor of HA-WBRT+M (p=0.012). The 6-month NCF failure rates were 69.1% (95% CI:61.8–75.3%) vs. 58.0% (95% CI:50.2–64.9%) for WBRT+M vs. HA-WBRT+M, respectively. After adjusting for stratification factors, HA-WBRT+M (hazard ratio (HR)=0.73, 95%CI:0.56–0.94, p=0.016) and age 61 years (HR=0.61, 95%CI:0.46–0.81, p=0.0006) remained significant. CONCLUSION: Preliminary analysis confirms that conformal avoidance of the neuro-regenerative hippocampal stem cell compartment during WBRT preserves neurocognitive function while achieving similar intracranial control and survival. Supported by grants UG1CA189867 (NCORP), U10CA180868 (NRG Oncology Operations), DCP from the National Cancer Institute.

NCOG-02. LONGITUDINAL AND PROSPECTIVE NEUROBEHAVIORAL OUTCOMES IN NEWLY-DIAGNOSED PRIMARY CNS LYMPHOMA PATIENTS TREATED WITH PRIMARY CRANIAL RADIOTHERAPY COMBINED WITH OR WITHOUT MTX-BASED CHEMOTHERAPY

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BACKGROUND: Primary central nervous system lymphoma (PCNSL) is an uncommon disease. Conventional treatment has consisted of either whole-brain radiotherapy (WBRT) or methotrexate (MTX)-based combined modality therapy combining chemotherapy and cranial irradiation. The addition of chemotherapy to cranial RT has significantly improved survival outcomes. However, delayed treatment-related cognitive sequelae have emerged as a significant debilitating complication of combined modality treatment in PCNSL patients, especially when effective treatment can result in disease control and greater survival. Furthermore, the specific contribution of the disease *per se* and various treatment modalities to cognitive impairment remains unclear because it is difficult to differentiate the individual neurotoxic effects of combined modalities when each can lead to cognitive dysfunctions respectively. Methods: A prospective observational cohort study with longitudinal assessments of neurobehavioral functions, neuroimaging, and activities of daily living in newly-diagnosed PCNSL patients was undertaken at our institute. Neurobehavioral outcomes were integrated into this prospective study and a battery of neuropsychological measures was used to evaluate neurocognitive functions (NCFs). The battery is composed of ten standardized NCF tests, representing four domains sensitive to disease and treatment effects (executive function, attention, verbal memory, psychomotor speed), and activities of daily living. RESULTS: Totally 15 patients with newly-diagnosed PCNSL including two cases with primary intraocular lymphoma were consecutively enrolled from February 2014 to January 2018. Comparing the differences in NCF scores between the baseline and post-treatment intervals, neurobehavioral outcomes consistently remained improving or in almost every domain evaluated in this study. Specifically, the scores of executive functions based on Paced Auditory Serial Addition Test (PACT) significantly improved between the baseline and post-chemoradiation assessment (Wilcoxon rank sum test, p = 0.016). CONCLUSIONS: Under the multidisciplinary treatment guidelines implemented at our institute, both improving neurobehavioral outcomes and maintaining oncological outcomes can be achieved.