**FINAL CATEGORY: CLINICAL RESEARCH METHODS**

**CLRM-01**

**SUMMARY OF VIRTUAL TUMOR BOARD PLATFORMS AND IMPLEMENTATION IN NEURO-ONCOLOGY**  
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**OBJECTIVE:** To report a summary of a systematic review of virtual tumor boards and their implementation in neuro-oncology.  
**BACKGROUND:** Virtual tumor board (VTB) platforms are an important aspect of cancer management. They enable easier access to a multidisciplinary team of experts. VTBs are an emerging resource across various cancer care networks in the United States.  
**DESIGN/METHODS:** We performed a systematic search of all VTBs incorporating a platform designed for this specific role. We reviewed UC Davis Health Care Center VTB, Genomet, Oncolens, Navify Tumor Board, Medical University of South Carolina Virtual Tumor Board, Procerus Oncology, Cancer Commons, Virtual Tumor Board, Virtual Tumor Board Tahoe Forest Cancer Center and MassiveBio.  
**RESULTS:** Summary data examined include year of launch, demographics, characteristics of cases, average response time, advantages, and how they handle protected health information.  
**CONCLUSIONS:** 30% of all VTBs examined launched in 2017. All had a HIPAA compliant online environment. Genomet VirtualBoard de-identifies all patient information; this is a virtual platform primarily focused on neuro-oncology cases. Cases involved a median of 5 specialists most commonly neuro-oncologists, neurosurgeons, radiation oncologists, molecular pathologists and neuroradiologists. Participants had an average of 23 cases reviewed. Case review revealed an age range from 6 months to 84 years [mean age 44.3 years] with 69.6% males and 30.4% females, 43.1% glioblastoma, 8.7% infiltrating glioma, <5% each pineoblastoma, melanoma, hemangioblastoma and pilocytic astrocytoma. Average response time observed in all cases was ≤24 hours. Detailed metrics for numbers/percent-ages for VTBs were not available for most others for time at submission. This will be updated at presentation.  
**CONCLUSIONS:** VTBs have allowed for quicker expert analysis of cases. This has resulted in an accelerated number of cases reviewed with a shortened communication time. More studies are needed to gain additional insight into user engagement metrics.

**CLRM-02**

**SINGLE CENTER EXPERIENCE OF DOPAMINE ANTAGONIST ONC-201 FOR RECURRENT H3K27M-MUTANT GliOBLASTOMA IN ADULTS**  
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**OBJECTIVE:** To report the single center experience of three adult subjects receiving ONC-201 as part of the ONC018 expanded access clinical trial [NCT03134131].  
**BACKGROUND:** ONC-201 is an oral investigational antagonist against the D2 dopamine receptor that has shown encouraging results for malignant gliomas harboring the H3K27M mutation in the H3 histone complex. Responses have been reported in pediatric subjects with such tumors. H3K27M tumors are generally located in the midline of the central nervous system which co-localize, for unknown reasons, with key dopaminergic pathways. An expanded access clinical trial (ONC018) was available to eligible patients allowing them access to this agent pending FDA review.  
**RESULTS:** We enrolled three subjects at our site with age range 18-44yrs, 2/3 female, residing in Norway, India and United states.  
**Tumor locations:** brainstem, corpus callosum and thalamus.  
**Pathology:** glioblastoma[3/3], MGMT methylated (2/3), IDH1 mutant (0/3), EGFR amplification (0/3) and ATRX (3/3).  
**Median change from baseline KPS:** ≤20% decrease; MDASI-2/3 experienced decrease from baseline [median 6%].Consistent with improved quality of life. No clinically significant laboratory abnormalities. No serious adverse events observed in any cases. All adverse events grade I-II.  
**CONCLUSIONS:** In three subjects with H3K27M-mutant malignant glioma that received ONC201 as part of this expanded access clinical trial, we found that study drug was quite tolerable. No serious adverse events nor radiographic responses were seen. Analyses of larger study cohort and additional randomized controlled trials are necessary to provide insight into the safety and efficacy of this agent for this patient population.

**CLRM-03**

**INCIDENCE OF INTRACRANIAL HEMORRHAGE IN GLIOMA PATIENTS WITH VENOUS THROMBOEMBOLISM CONVERTED FROM LMWH TO APIXABAN**  
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Venous Thromboembolism (VTE) occurs in approximately 15-30% of patients with glioma.1,2 who are treated with therapeutic anticoagulants. Anticoagulation treatment increases the incidence of intracranial hemorrhage (ICH) with variable incidence between studies 1.9% to 20% 3-6. The “common practice” treatment for VTE in glioma patients includes subcutaneous administration of low molecular weight heparin (LMWH, enoxaparin) injection, which requires daily self-injection. Switching glioma patients with VTE from LMWH to oral anticoagulants would limit the difficulties and the inconvenience of daily self-injection in primary brain tumor patients and decrease the room for error in administering the dose along and the risk for heparin induced thrombocytopenia.7 The goal of this project is to evaluate the incidence of intracranial hemorrhage in glioma patients with VTE converted from LMWH to Apixaban. We hypothesize that patients with brain tumors and Venous Thromboembolism can be converted safely from LMWH to Apixaban. To examine this hypothesis, we will enroll adult patients with pathologically confirmed supra-tentorial glioma and venous thromboembolism. Patients must have been treated with LMWH for ≥ 5 days. We will exclude patients with bleeding diathesis, severe hypersensitivity to Apixaban or pregnant or unable to provide informed consent. To assess the validity of our hypothesis: Primary Objective: To estimate the incidence of ICH in glioma patients with history of VTE after the conversion from LMWH to Apixaban. Secondary Objective: To estimate the incidence of recurrent VTE in glioma patients with history of VTE after the conversion from LMWH to oral Apixaban. To our knowledge, this is the first of its kind study to estimate the risk of ICH in glioma patients with VTE treated with oral anti-coagulants. Successful completion of our trial will provide answers to an important clinical question that could allow our patients using more convenient yet effective treatment by establishing and implementation of best practices.

**CLRM-05**

**FEASIBILITY OF EVALUATING ABEIMACILIB NEUROPHARMACOKINETICS OF DIFFUSE MIDLINE GLIOMA USING INTRATUMORAL MICRODIALYSIS**  
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**INTRODUCTION:** Diffuse midline gliomas are the most aggressive brain tumors of childhood and young adults, with documented 2 year survival rates of <10%. Treatment failure is due in part to the presence of the blood-brain barrier (BBB), which limits permeability of varied agents. Efforts to evaluate drug delivery across the BBB in midline gliomas have been restricted to post biopsy specimens. Intracerebral microdialysis sampling of cortical tissue has been shown to be a highly effective tool in determining neuropharmacokinetics in adult brain tumors. METHODS: All participants will take abemaciclib pre-operatively for 4.5 days at twice daily dosing. A maximally safe surgical resection for cortical high grade glioma must be treated with LMWH for ≥ 5 days. We will exclude patients with bleeding diathesis, severe hypersensitivity to Apixaban or pregnant or unable to provide informed consent. To assess the validity of our hypothesis: Primary Objective: To estimate the incidence of ICH in glioma patients with history of VTE after the conversion from LMWH to Apixaban. Secondary Objective: To estimate the incidence of recurrent VTE in glioma patients with history of VTE after the conversion from LMWH to oral Apixaban. To our knowledge, this is the first of its kind study to estimate the risk of ICH in glioma patients with VTE treated with oral anti-coagulants. Successful completion of our trial will provide answers to an important clinical question that could allow our patients using more convenient yet effective treatment by establishing and implementation of best practices.
sequencing and PDX modeling. CONCLUSION: We propose a trial using clinical microdialysis, placed in diffuse midline glioma tissue post biopsy, as an experimental research tool, to assess CNS drug entry and targeted inhibition with ablative therapy. It will be the first of its kind, focused on the dynamic nature of CNS drug delivery with the overall intent to inform future clinical therapies.

CLRM-06
PROSPECTIVE CLINICAL STUDY OF CONVENTIONALLY FRACTIONATED CONCURRENT CHEMORADIOThERAPY AND HYPOFRACTIONATED CONCURRENT CHEMORadioThERAPY AFTER THE SURGERY OF HIGH-GRADE GLIOMAS
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PURPOSE: To observe and evaluate the efficacy and safety of conventional fractionated concurrent chemoradiotherapy and hypofractionated concurrent chemoradiotherapy within 1 month after surgery, and received concurrent temozolomide 75 mg/m2 during radiotherapy until the end of radiotherapy. Sequential temozolomide chemotherapy at 200 mg/m2 for at least 6 cycles. All patients were randomly divided into groups, one group was given conventional fractional irradiation, 60Gy/30f in high-risk areas, 46Gy/23f in low-risk areas, and the other group was given low-fractionated irradiation, 53Gy/18f in high-risk areas, and 53Gy/15f in low-risk areas 43Gy/15f. The overall survival (OS), progression-free survival (PFS), radiation-induced cerebral edema and radiation-induced brain necrosis were evaluated. RESULT: As of December 1, 2022, a total of 60 patients were enrolled, including 30 in the conventional fractionation treatment group and 30 in the hypofractionated treatment group. At present, 58 patients survived and 2 died, 2 in the conventional fractionation group, one due to tumor recurrence and one due to cardiac accident; 7 patients recurred, including 4 in the conventional fractionation group and 3 in the low fractionation group. Radiotherapy cerebral edema occurred in 9 cases, 6 cases in the hypofractionated group and 3 cases in the conventional fractionation group, all of which were completely relieved after dehydration with mannitol, which did not affect the progress of radiotherapy. Radiation necrosis occurred during follow-up. CONCLUSION: Compared with the standard stupp regimen, using 53Gy/15f in the high-risk area and 43Gy/15f in the low-risk area as an adjuvant therapy with concurrent temozolomide and sequential temozolomide, there was no increased risk of disease recurrence, no increased risk of death, and no increased risk of death.

CLRM-07
A MULTIVARIATE RETROSPECTIVE ANALYSIS OF 159 PATIENTS WITH HIGH-GRADE GLIOMAS: OVERALL SURVIVAL, PROGRESSION-FREE SURVIVAL, AND PROGNOSTIC FACTORS
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BACKGROUND AND PURPOSE: High-grade gliomas are highly malignant, aggressive, high incidence rate, and mortality. The purpose of this study was to analyze retrospectively and identify prognostic factors of patients with high-grade gliomas diagnosed by biopsy or postoperative pathological examination. METHODS: In this retrospective study, we analyzed the patient's demographic data, tumor characteristics, treatment approaches, immunocytochemistry results, the overall survival (OS) time, and the progression-free survival (PFS) time in a series of 159 histologically proven high-grade gliomas recruited from January 2011 to December 2019. OS time and PFS time were analyzed by Kaplan-Meier survival analysis, and the progression-free survival (PFS) time in a series of 159 histologically proven high-grade gliomas recruited from January 2011 to December 2019. OS time and PFS time were analyzed by Kaplan-Meier survival analysis. RESULT: Survival analysis showed that an OS of 84.90% (P < 0.01), 147 patients underwent concurrent chemoradiotherapy and 80 of them died; 12 patients did not undergo concurrent chemoradiotherapy and 10 died (P = 0.03). There were statistically significant differences in the prognostic impact of Ki-67 expression, MGMT, IDH1R132H and p53 mutations by immunohistochemistry (P = 0.001; P = 0.016; P = 0.003; and P = 0.021, respectively). Similarly, we concluded that different grades, age, pathological classification, and p53 mutations by immunohistochemistry were statistically significantly associated with PFS (P < 0.01; P = 0.004; P = 0.003; P = 0.001; and P = 0.028). CONCLUSIONS: Tumor grade and concurrent chemoradiotherapy after surgery were independent prognostic factors affecting patients' survival, and grade was also an independent factor affecting PFS.

CLRM-08
TARGETING IMMUNE-PAYLOAD TO THE GlioBLASTOMA TUMOR MICROENVIRONMENT USING A MACROPHAGE-BASED TREATMENT RELYING ON AUTOLOGOUS, GENETICALLY MODIFIED, HEMATOPOIETIC STEM CELL-BASED THERAPY: THE TEM-GBM STUDY (NCT03866109)
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We developed an autologous hematopoietic stem cell-based platform designed to deliver IFNα, by a transcriptional and post-transcriptional control mechanism mediated by miRNA target sequences, specifically into the tumor microenvironment (TME) via a retroviral vector (Temferon). As of Feb 2022, 3 escalating doses of Temferon (0.5-2.0x10^6/kg) were tested across 15 newly diagnosed, unmethylated MGMT GBM patients assigned to 5 cohorts. Follow-up from surgery is 6–28mo (2–25mo after Temferon). To date, no DLTs have been identified. 1,3m after the administration of the highest tested dose, the hematopoietic system of Temferon-treated patients was composed of up to 30% of CD14+ modified cells. Temferon-derived progeny persisted, albeit at lower levels, up to 18mo (longest time of assessment). Despite the substantial proportion of engineered cells, low concentrations of IFNαs were detected in the plasma and in the CSF, indicating tight regulation of transgene expression. SAEs were mostly attributed to conditioning chemotherapy (infections) or disease progression (seizures). 1SUSAR (persistent GGT elevation) occurred. Median OS is 13mo from surgery. Homing of transduced cells to the tumor was demonstrated by the presence of gene-marked cells in the 2nd surgery specimens of 3 out 4 pts belonging to low dose cohorts. Single-cell RNA seq of the TME highlighted a Temferon signature associated with the induction IFNα response genes and macrophage polarization. Potential long-term benefit with Temferon was identified in a patient from cohort 3, who had PD at D=120 with two distant enhancing lesions, and increased tumor necrosis. 1y following Temferon, with no 2nd-line therapy added, there was approximately 50% reduction in enhancing tumor volume compared to D=180 with a stable clinical and imaging picture thereafter. The results provide initial evidence of Temferon’s potential to modulate the TME of GBM patients, and anecdotal evidence for long lasting effects of Temferon in prevention of disease progression.