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 abemaciclib. These studies will be the first of their 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 for adjuvant treatment of newly treated high-grade glioma. METHOD: For newly treated patients with high-grade gliomas with WHO grade III-IV, all patients started 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/15f 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 31, 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. Radiation 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. No 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 with log-rank test and found the independent factors by using Cox regression analysis. RESULTS: Survival analysis showed that an OS of 84.90%, 55.35% and 13.20% was observed at 1, 2 and 5 years, respectively. And a PFS of 56.6%, 25.26% and 3.14% was observed at 1, 2 and 5 years, respectively. The mean OS was 52.73 months and mOS was 35 months. Univariate analysis showed that postoperative pathological classification and grade and age were statistically significant for patient outcome ($P < 0.01$). 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, Ki-67 and IDH1R132H expression by immunohistochemistry were statistically significantly associated with PFS ($P < 0.01$; $P = 0.004$; $P = 0.003$; $P = 0.001$; $P = 0.028$). 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 IFNa, by a transcriptional and post-transcriptional control mechanism mediated by miRNA target sequences, specifically into the tumor microenvironment (TME) via Tie-2 expressing monocytes (Temferon). As of Feb 2022, 3 escalating doses of Temferon (0.5-2.0x106/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. As expected, 1mo 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 analysis). Despite the substantial proportion of engineered cells, very low concentrations of IFNα 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 15mo 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 IFNa responsive genes and macrophage repolarization. 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 40% 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.

CLRM-09

FIRST-LINE TUMOR TREATING FIELDS (200 KHZ) THERAPY FOR NEWLY-DIAGNOSED GLIOBLASTOMA: THE PHASE 3 TRIDENT TRIAL (EF-32)

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BACKGROUND: Tumor Treating Fields therapy (TTFields; 200 kHz) comprise alternating electric fields that disrupt cancer cell division, and is approved for newly diagnosed glioblastoma (ndGBM), recurrent GBM and mesothelioma. In the phase 3 EF-14 trial, TTFields/temozolomide