trial evaluating it for recurrent HGGs. OBJECTIVE: Determine whether CSC-targeted cytotoxic agents selected by ChemoID assay-guided therapy improves survival in patients with recurrent HGG. DESIGN, SETTING, AND PARTICIPANTS: In this parallel-group, randomized, phase-3 clinical trial, patients at 13 clinical sites in the USA with grade-III/IV recurrent glioma (2016 WHO guidelines) were randomized 1:1 to either ChemoID assay-guided therapy or physician-choice therapy, and then treated and followed until unacceptable toxic effects, hospice, or death. MAIN OUTCOMES AND MEASURES: The primary endpoint was overall survival (OS). RESULTS. Combined median follow-up was 9 months. Median OS (mOS) was 12.5 months (95% CI, 10.2-14.7) in the ChemoID assay-guided group vs 9 months (95% CI, 4.2-13.8) in the physician-choice group (log-rank P = .010). Risk of death was significantly lower in the ChemoID assay group (HR = 0.44; 95% CI, 0.24-0.81; P = .008). Median progression free survival (PFS) was 10.1 vs 3.5 months (95% CI, 4.8-15.4 vs 1.9-5.1) (HR, 0.25; 95% CI, 0.14-0.44; P < .001). CONCLUSIONS AND RELEVANCE: Primary endpoint was met in this randomized clinical trial. The mOS was 3.5 months longer in the ChemoID assay-guided group vs the physician-choice group.

SYST-02

PHASE ⅡB CLINICAL TRIAL OF NEOADJUVANT CHEMOTHERAPY REVERSING GLIOMA STEM CELLS CHEMORESISTANCE IN NEWLY DIAGNOSED GBM WITH MGMT PROMOTER UNMETHYLATION

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PURPOSE: To evaluate clinical efficacy and safety of combination of nicardipine and valproic acid on temozolomide (TMZ) neoadjuvant chemotherapy targeting on glioma stem cells (GSCs) in newly diagnosed glioblastoma multiforme (GBM) patients with O^6-methylguanine-DNA-methyltransferase (MGMT) promoter unmethylation. METHODS: From June 2018 to April 2021, newly diagnosed GBM patients after tumor surgical removal and concurrent radio-chemotherapy with TMZ, with MGMT promoter unmethylation were randomly assigned to two groups. The control group was applied standard TMZ regimen. The trial group was administered standard TMZ regimen, plus nicardipine(20mg/d) and valproic acid (1.2g/d) as neoadjuvant treatment against GSCs chemoresistance. The relevant treatment data and adverse reactions of the patients were collected, Karnofsky performance status (KPS) score, progression-free survival (PFS) and overall survival (OS) were evaluated during patient follow-up. RESULTS: 33 patients were enrolled in this study, eighteen patients were randomly assigned in the trial group and 15 patients were in the control group. There was no statistical difference in gender composition, age, degree of surgical resection, or KPS score before treatment between the two groups. The median progression-free survival (mPFS) in the trial group was 10.8 months (95%*CI* 5.81-15.79 month), and the mPFS in the control group was 7.1 months (95%*CI* 5.12-9.08 month), which was a statistically difference (Log-Rank test P=0.033). The median overall survival (mOS) increased from 12.1 months (95%*CI* 9.18-15.00 month) in the control group to 15.7 months (95%*CI* 7.67-23.73 month) in the trial group (Log-Rank test *P*=0.015). There was no statistically significant difference in the incidence of adverse reactions between the two groups, and there were no treatment regimen related deaths. CONCLUSIONS: TMZ combined with neoadjuvant of nicardipine and valproic acid against GSCs chemoresistance can prolong the survival time of patients who was newly diagnosed glioblastoma with MGMT promoter unmethylation. The preferred regimen can be applied safely without serious adverse events, which deserved further multi-center clinical investigations.

SYST-03

INCIDENCE AND SURVIVAL OF PATIENTS WITH INTRACRANIAL METASTATIC DISEASE AND ERBB2-POSITIVE GASTROINTESTINAL CANCERS: A RETROSPECTIVE COHORT STUDY

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BACKGROUND: Intracranial metastatic disease (IMD) is a mortality-driving complication of gastrointestinal (GI) cancers. In breast cancer, ERBB2 positivity is associated with shorter overall survival (OS) and increased risk of IMD, and while ERBB2 status is relevant in primary GI cancer, no study has directly assessed the relationship of ERBB2 status and IMD in these patients. METHODS: Records for adult patients with GI cancer and IMD, treated with ERBB2-therapy between 2005 and 2018 were retrieved from ICES. Baseline characteristics were compared between subcohorts stratified by IMD and ERBB2 statuses. Kaplan-Meier and Cox regression analyses were performed to estimate survival. RESULTS: Records for 99,256 patients with GI cancer were collected, and IMD was diagnosed in 2002 patients. The highest IMD incidence rate was among patients with esophageal cancer (5.5%). Among patients with ERBB2+ disease, 306 had gastric (9 IMD), 168 esophageal (15 IMD), and 17 colorectal cancer. Diagnosis of IMD was associated with shorter OS among patients with colorectal (HR 3.0; 95% CI 2.9–3.2), gastric (HR 1.7; 95% CI, 1.5–1.9), and esophageal cancers (HR 1.2; 95% CI, 1.1–1.4). Post-IMD ERBB2-targeted therapy was not associated with OS among patients with ERBB2+ esophageal (HR 0.5; 95% CI, 0.2–1.2; n = 15) or gastric cancer (HR 0; 95% CI 0–Inf; n = 9). CONCLUSION: Our study assessed patients with ERBB2+ GI cancer and IMD. Diagnosis of IMD was associated with shorter survival in gastric, esophageal, and colorectal cancers. Post-IMD ERBB2 therapy was not associated with OS, and IMD diagnosis was associated with prolonged survival in patients with stage 4 ERBB2+ disease, although interpretation of these results is complicated by small sample size and selection bias. Our results motivate increased reporting and inclusion of patients with ERBB2+ GI cancers in clinical trials.

SYST-04

PRELIMINARY REPORT OF A CLINICAL TRIAL EVALUATING THE SAFETY AND EFFICIENCY OF NEOADJUVANT CAMRELIZUMAB AND APATINIB IN PATIENTS WITH RECURRENT HIGH-GRADE GLIOMAS: A PROSPECTIVE, PHASE II, SINGLE-ARM STUDY

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High-grade glioma is the most common malignant primary brain tumor in the central nervous system. Multiple strategies such as surgery, radiotherapy, and chemotherapy have been used, but the prognosis of patients with high-grade glioma remains poor. No standard treatment exists for recurrent gliomas; however, combination therapies of programmed cell death protein 1 blockades with antiangiogenic agents have demonstrated promising effects in different solid tumors. We have initiated a clinical trial designed to evaluate the safety and efficiency of neoadjuvant therapy using camrelizumab and apatinib in patients with recurrent highgrade gliomas. In this prospective, Phase II, singlearm study, patients with recurrent highgrade gliomas will receive singledose intravenous injection of camrelizumab (200 mg) and daily oral administration of apatinib (250 mg/day for 7 days) 14 days before surgery for recurrent tumor. Sequential therapy will begin 2 weeks after surgery with the biweekly injection of camrelizumab and 4 weeks after surgery with the daily administration of apatinib. Treatment of camrelizumab and apatinib will be continued until disease progression or unacceptable toxicity or death. The trial is planned to enroll 30 patients. Up-to date (March 31, 2022), 12 patients had been enrolled, in which, 9 were GBM. Three patients died, while 4 cases on trial more than 6 months, the longest already 1 year. Although an evaluation is still impossible to be conducted yet, some patients have shown a promising outcome. We will present updated results on the meeting. These preliminary data suggest that this study would be worthwhile. This study was approved by the Ethics Committee of Sun Yatsen University Cancer Center (Guangzhou, China; approval No. SLB202014901). This study was registered with ClinicalTrials.gov under identifier NCT04588987.

SYST-05

OPTIMIZING HER2-TARGETED THERAPIES (TT) FOR BREAST CANCER (BC) LEPTOMENINGEAL METASTASES (LM): A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: LM is a debilitating condition associated with metastatic cancers, including BC. When oncogenic drivers are identified, TT represents an appealing therapeutic strategy. However, the efficacy of TT for LM is unknown as LM patients are routinely omitted from clinical trials. METHODS: We conducted a systematic review and meta-analysis of individual patient data to evaluate the effectiveness of HER2-TT in HER2+ BCLM in accordance with PRISMA guidelines. TTs evaluated included trastuzumab (intrathecal (IT) or intravenous (IV)), trastuzumab-