

(RP2D) for further study. Toxicity is assessed based on NCI CTCAEv5 and tumor response is assessed by RECIST 1.1. CNS exposure is evaluated in patients via CSF collection with confirmed CNS disease involvement.

TRLS-07. INTRACAVITARY CARRIER-EMBEDDED Cs131 BRACHYTHERAPY FOR RECURRENT BRAIN METASTASES: A RANDOMIZED PHASE II STUDY

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BACKGROUND: The salvage treatment of recurrent brain metastases after failed irradiation is a clinical challenge. Adjuvant SRS is standard of care for resected brain metastases in the upfront post-resection setting given a significant local control advantage over surgery alone. However, the role of reirradiation following salvage resection of recurrent post-irradiation metastases is unclear owing to both reduced efficacy of subsequent courses of external beam radiation, and likely increased risk of radiation injury. Intracavitary cesium 131 (Cs131) brachytherapy offers a highly conformal adjunct radiation option that we hypothesize may allow for improved local control while also theoretically conveying a low risk of radiation necrosis. In this randomized controlled study, we aim to define the potential benefits and risks of resection plus permanently implanted, carrier-embedded intracavitary Cs131 brachytherapy versus conventional care (surgery alone). **METHODS:** This is a single-center randomized controlled study of patients undergoing resection of recurrent, previously-irradiated brain metastases. Exclusion criteria include prior in-field infection, prior radiation >100Gy (in 2Gy fraction equivalents), >5 additional active or untreated CNS lesions, or leptomeningeal carcinomatosis. Subjects are randomized 1:1 to undergo either surgery with placement of Cs131 brachytherapy or surgery alone. The primary endpoint is freedom from treated-site progression at 9 months. Secondary endpoints include wound complications at 3 months and time to local retreatment at the index site, and exploratory objectives include neurocognitive function prior to surgery and at 3 and 12 months postoperatively, with correlative analyses of the previously irradiated brain metastasis tissue. Accrual began on December 24, 2020 and 5 of a planned 76 patients have enrolled. This is the first randomized controlled trial of surgery plus permanently implanted intracavitary Cs131 brachytherapy versus surgery alone for recurrent brain metastases.

ClinicalTrials.gov Identifier: NCT04690348

LEPTOMENINGEAL DISEASE

LMD-01. QUANTIFYING INTRATHECAL DRUG DELIVERY UTILIZING PROGRAMMABLE VENTRICULOPERITONEAL SHUNTS

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BACKGROUND: Programmable ventriculoperitoneal shunts (pVP shunts) are increasingly utilized for intraventricular chemotherapy, radioimmunotherapy, and/or cellular therapy. Shunt adjustments allow optimization of thecal space drug concentrations with minimization in the peritoneum. Drug delivery quantification using several types of pVP shunts has not been reported. **METHODS:** We performed a retrospective analysis on patients with CNS tumors and pVP shunts at Memorial Sloan Kettering Cancer Center from 2003–2020, noting shunt model. CSF flow through the pVP shunt was evaluated using In-111-DTPA scintigraphy at approximately 4 and 24 hours after injection. pVP shunts were calibrated pre-injection to minimize peritoneal flow and re-calibrated to baseline setting 4–5 hours following injection. Scintigraphy studies quantified ventricular-theal and peritoneal drug activity at these 2 time points. **RESULTS:** Twenty-one CSF flow studies were administered to 15 patients, ages 1–27 years. Diagnoses included medulloblastoma (N=10), metastatic neuroblastoma (N=3), pineoblastoma (N=1), and choroid plexus carcinoma (N=1). Models of pVP shunts included Aesculap Miethke proGAV (N=3), Aesculap Miethke proGAV2.0 (N=3), Codman HAKIM (N=2), Codman Certas Plus (N=1), Medtronic STRATA (N= 5), and Sophysa Polaris (N= 1). All 21 studies (100%) demonstrated ventriculo-theal drug activity. 29% (6 of 21) of the studies had no peritoneal uptake visible by imaging. 73% (16 of 21) of the studies had minimal peritoneal uptake (<12%), and 24% (5 of 21) demonstrated moderate peritoneal uptake (12–37%). Models of pVP shunts measuring minimal to no peritoneal uptake included: Aesculap Miethke proGAV (N=2), Aesculap Miethke proGAV2.0 (N=3), Codman HAKIM (N=2), Codman Certas Plus (N=1), Medtronic STRATA (N= 3), and Sophysa Polaris (N= 1).

CONCLUSIONS: pVP shunts successfully deliver drugs to the ventriculo-theal space with 80% of studies having minimal (<12%) peritoneal drug activity. Though efficacy varies by shunt model, low numbers preclude conclusions regarding model superiority. CSF flow scintigraphy studies reliably assess drug distribution.

LMD-02. CEREBROSPINAL FLUID DIVERSION FOR METASTATIC LEPTOMENINGEAL CARCINOMATOSIS: PALLIATIVE, PROCEDURAL AND ONCOLOGIC OUTCOMES

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BACKGROUND: Leptomeningeal disease (LMD) occurs in 3–5% of patients with solid metastatic tumors and often portends a severe prognosis including symptomatic hydrocephalus and intracranial hypertension. Cerebrospinal fluid (CSF) shunting can provide symptomatic relief in this patient subset; however, few studies have examined the role of shunting in the palliation, prognosis and overall oncologic care of these patients. **OBJECTIVE:** To identify and evaluate risk factors associated with prognosis after CSF diversion and assess surgical, symptomatic and oncologic outcomes in this population. **METHODS:** A retrospective study was conducted on patients with solid-malignancy LMD treated with a shunt at an NCI-designated Comprehensive Cancer Center between 2010–2019. **RESULTS:** One hundred and ninety patients with metastatic LMD underwent CSF diversion. Overall survival was 4.14 months from LMD diagnosis (95% CI:3.29–4.70) and 2.43 months (95% CI:2.01–3.09) from shunting. KPS at time of shunting and BrM number at LMD diagnosis demonstrated significant associations with survival (HR=0.66; 95% CI[0.51–0.86], p=0.002; HR=1.40; 95% CI[1.01–1.93] per 10 BrM, p=0.04, respectively). Eighty-three percent of patients experienced symptomatic relief, and 79% were discharged home or to rehabilitation facilities post-shunting. Post-shunt, 56% of patients received additional systemic therapy or started or completed WBRT. Complications included infection (5%), symptomatic subdural hygroma/hematoma (6.3%), and shunt externalization/removal/repair (8%). Abdominal seeding was not identified. **CONCLUSIONS:** CSF diversion for LMD with hydrocephalus and intracranial hypertension secondary to metastasis can achieve symptomatic relief, hospital discharge, and return to further oncologic therapy, with a complication profile unique to this pathophysiology. However, decision-making in this population must incorporate end-of-life goals of care given limited prognosis.

LMD-03. SINGLE CELL ANALYSIS REVEALS HOW THERAPY REMODELS THE TUMOR MICROENVIRONMENT IN MELANOMA CNS METASTASES AND UNCOVERS A NOVEL PREDICTOR OF IMPROVED SURVIVAL

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We interrogated the microenvironment of 43 clinical samples from melanoma skin, brain (MBM) and leptomeningeal metastases (LMM) using single-cell RNA-seq analysis to determine how therapeutic intervention shaped the immune environment and affected patient survival. LMM is a poorly-characterized, devastating complication of late-stage disease, typically refractory to treatment and associated with dismal survival time. Analysis of serial specimens over the course of therapy demonstrated reductions in melanoma cells and macrophages, coupled with increased levels of T cells and dendritic cells in the CSF of a rare extraordinary responder, whereas typical poor survivors showed no improvement in T cell responses. In MBM patients, both targeted therapy and immunotherapy was associated with increased immune infiltrate. Treatment with targeted therapy was associated with an enrichment of CD8 T cells, while immunotherapy was associated with a more diverse lymphocyte landscape and higher numbers of antibody-producing cells. These findings were confirmed by multiplex-IF staining of patient specimens and using an immune-competent mouse model of MBM. Interestingly, a history of prior radiation therapy was associated with a diminished myeloid compartment. Although immune infiltrate was significantly lower in the brain compared to skin tumors, the phenotypic make-up of the lymphocyte compartment was quite similar, suggesting that the immune cells may have trafficked from the periphery to the brain post-therapy. Correlation analysis across the entire immune landscape identified the presence of a rare, novel population of dendritic cells (DC3s) to be correlated with increased overall survival, regardless of disease site/treatment. The presence of DC3s positively regulated the immune environment of both patient samples and preclinical