growing lesions (n >1) at time of intervention (50.0%) versus those treated with surgery (15.2%) (p< 0.05). Likewise, pre-treatment KPS was lower in the bevacizumab cohort (median: 60) vs the surgery cohort (median: 90) (p< 0.05). Patients treated with bevacizumab demonstrated significantly decreased PFS (%PFS at 1-year 16.7% vs 86.7% and 87.8% for craniotomy and LITT, respectively; %PFS at 2-years 0% vs 86.7% and 73.2% for craniotomy and LITT, respectively, p < 0.05). Similar results were observed for OS (%OS at 1-year for bevacizumab 33.3% vs 93.3% and 73.8% for craniotomy and LITT, respectively; %OS at 2-years for bevacizumab 11.1% vs 64.6% and 63.2% for craniotomy and LITT, respectively, p< 0.05). CONCLUSIONS: Preliminary analysis shows that bevacizumab therapy in our institution is being chosen for patients with lower KPS and multiple regrowing lesions while surgical intervention is being chosen for patients with good KPS and single, symptomatic regrowing lesions. While the comparative outcomes after bevacizumab appear to be significantly worse than surgical management, it remains unknown if the difference is more related to its true efficacy or the significant discrepancy between the comparison groups.

MLTI-07. PREOPERATIVE VERSUS POSTOPERATIVE STEREOTACTIC RADIOSURGERY FOR LARGE BRAIN METASTASES: AN INTERNATIONAL META-ANALYSIS

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PURPOSE: Preoperative stereotactic radiosurgery (SRS) for symptomatic brain metastases has arisen as a therapeutic option for patients with brain lesions, potentially reducing radionecrosis risk, leptomeningeal disease risk, as well as delays in systemic therapy after craniotomy. The purpose of our work is to analyze the current evidence regarding 1-year local control (LC) and RN rates in the preoperative and postoperative settings. METHODS AND MATERIALS: Population, Intervention, Control, Outcomes, Study Design/Preferred Reporting Items for Systematic Reviews and Meta-analyses and Meta-analysis of Observational Studies in Epidemiology guidelines were used to select articles in which patients had "large" brain metastases (>4 cm3 or >2 cm in diameter) solely treated with preoperative or postoperative SRS and 1-year LC and/or rates of RN reported. Radiosurgery was stratified by timing: preoperatively or postoperatively. Random effects meta-analyses using timing of SRS relative to surgery as covariates were conducted. Meta-regression and Wald-type tests were used to determine the effect of increasing tumor size on the summary estimate, where the null hypothesis was rejected for p < 0.05. RESULTS: Fifteen studies were included (of 314 screened), published between 2012 and 2018 with 854 brain metastases. Preoperative SRS was delivered in 229 lesions. The 1-year LC random effects estimate was 79.1% (95% confidence interval [CI]: 55.9–95.0%; *I2* = 80%) for preoperative SRS and 80.5% (95% CI: 66.3–91.5%; *I2* = 93%) for postoperative SRS (p=0.9). Radionecrosis incidence random effects estimate was 2.1% (95% CI: 0.1–8.6%; *I2* = 36%) for preoperative SRS and 6.3% (95% CI: 1.1–15.4%; *I2* = 90%) for postoperative SRS (p=0.52). CONCLUSIONS: Rates of 1-year LC and RN incidence are similar after preoperative SRS as compared to postoperative SRS for large brain metastases. Results from ongoing prospective clinical trials studying preoperative SRS are important to further investigate these two techniques.

MLTI-08. AN EXCEPTIONAL INTRACRANIAL RESPONSE TO REPEAT RADIATION AND IMMUNOTHERAPY IN A PATIENT WITH METASTATIC, POORLY DIFFERENTIATED ADENOCARCINOMA OF THE LUNG

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We report an unusual case of a long-term survivor of metastatic, poorly differentiated adenocarcinoma of the lung (EGFR- ALK-) who developed intracranial disease after definitive treatment of a stage IIIB lung cancer. He received a complex course of RT which began with SRS to his intracranial disease in 2012 and included: brainstem (pontine) mass, left parietal mass, left frontal, left lateral temporal, and left insular lesions. The left temporal mass progressed and was resected. Subsequently, SRS was given to a right anterior frontal lesion. Additional SRS was given to progressive right superior frontal mass & left temporal tumor bed was given fractionated RT to the left temporal tumor bed. Later, he developed bilateral cerebellar masses and right-sided progression. More SRS was given to right frontal area, and then to bilateral cerebellar lesions. Surprisingly, he did well neurologically until seizures developed. His repeat biopsy was sent for NGS and noted to be PDL1+, APC mutated, and KRAS mutated. This gentleman was started on pembrolizumab in May 2016. Due to colitis, his therapy stopped in January 2017. His colitis progressed such that immunotherapy could not be restarted. Now, after observation only for the past 2.5 years. his disease has disappeared. He is doing well neurologically. We propose that the use of radiation and immunotherapy worked to produce an exceptional, durable response.

MLTI-09. UNDERWEIGHT AND WEIGHT LOSS ARE PREDICTORS OF POOR OUTCOME IN PATIENTS WITH BRAIN METASTASIS

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BACKGROUND: Despite increased risk of comorbidities, overweight may be associated with improved outcome in patients with metastatic cancer. Conversely, tumor cachexia has been identified as a negative predictor of outcome in patients with brain metastasis (BM) from lung cancer. Here we evaluate the association of abnormal body mass index (BMI) and weight change with outcome in patients with BM from different primary tumors. METHODS: Patients with a diagnosis of BM diagnosed and treated at the University Hospital Zurich (n=703) were assessed for associations of BMI, weight change, comorbidities and survival. RESULTS: Compared with patients with normal BMI of 18.5–24.9 kg/m2 who experienced a median overall survival (OS) of 9 months (95% confidence interval (CI) 7.5–10.5), OS was inferior in patients with BMI< 18.5 kg/m2 (OS 6 months, 95% CI 1.6–10.3, p=0.04), but superior in patients with BMI >25 kg/m2 (OS 13 months, 95% CI 11.0–15.0; p=0.033). For patients with documented weight course (n=173 of 703), we report a median relative weight loss of 5% within the first 6 months of BM diagnosis (95% CI 3.3–6.5). Reduction above the median was associated with an unfavorable outcome in this subgroup (weight loss ≧5% 22.0 months, 95% CI 19.2–24.8; weight loss < 5% 14.0 months, 95% CI 11.9–16.). CONCLUSIONS: Despite being associated with a worse cardiovascular risk profile, high BMI is associated with preferable and underweight with poor outcome in BM patients. Conversely, weight loss above median may be a predictor of poor outcome. Future studies need to address the question whether vigorous treatment of tumor cachexia, e.g. by specific nutrition management, might improve outcome of BM patients. In contrast, regimens that are associated with weight loss such as ketogenic diet may be detrimental.

MLTI-10. ESTABLISHMENT OF A MULTIDISCIPLINARY BRAIN METASTASIS CLINIC TO FACILITATE PATIENT-CENTERED CARE AND COORDINATED RESEARCH

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BACKGROUND: ~30% cancer patients develop brain metastases (BM), reflected by ~1600 BM patients treated at MD Anderson Cancer Center annually. With advances in systemic therapy and extracranial disease control, BM is a growing challenge. Multi-disciplinary BM management is critical and complex requiring coordination of multiple oncology sub-specialties. There is limited data on pragmatic clinic models to streamline and advance care. METHODS: Recognizing deficiency in BM treatment and research, a steering committee was formed at MDACC to establish an interdisciplinary BM clinic (BMC), with a multi-disciplinary BM research retreat held in 2016. The goal of BMC was to centralize patient referrals, improve patient outcomes and experience, and advance research by developing clinical trials and biomarker discovery programs. Meetings were held to address BMC format, workflow, EMR integration, data collection infrastructure, and staffing model. RESULTS: MDACC BMC clinic opened in 01/2019 with two half-day clinics staffed by neurosurgery, neuro-radiation oncology, neuro-radiology and medical/neuro oncology. A dedicated advanced practice provider screens the referrals according to a well-developed algorithm. A multidisciplinary conference is held immediately before each clinic where patient images are reviewed, cases are discussed and consensus recommendations are developed. The treatment plan and follow up appointments are arranged at the completion of the clinic visit to expedite care.

~50 patients have been seen with excellent patient satisfaction response and reduced time to treatment. ~20% patients had major change in treatment plan following multi-disciplinary evaluation. Additional efforts to develop a central BM database along with clinical and translational research programs are on-going. CONCLUSIONS: Establishment of a multi-disciplinary BMC to facilitate care and centralize research programs addresses a critical need for coordinated patient-centered BM management. This endeavor has enhanced patient experience through multi-specialty collaboration. Our program demonstrates the feasibility and effectiveness of a dedicated BMC in the treatment of this complex patient population.

MLTI-11. IMPLANTABLE POLYMERIC BCNU AS AN ADJUNCT TO SURGERY FOR METASTATIC INTRACRANIAL DISEASE

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SUMMARY: One hundred and thirty cases of craniotomy for tumor utilizing BCNU implantable chemotherapy were performed by the authors between including 23 cases for metastatic intracranial disease. The series included 12 woman and 11 men with an average age of 56.9 years. The diagnoses were as follows: non-small lung carcinoma (13), breast cancer (6), small-cell lung cancer (1), colon cancer (1), unknown primary (2). Patients undergoing resection plus implantable chemotherapy following whole brain radiotherapy (5 patients) or following stereotactic radiosurgery (5 patients) were the most common. Only patient developed possible local recurrence (3%). Complications included two cerebrospinal fluid leaks with associated complications requiring reoperations (11%) both following whole brain radiotherapy and 3 patients (17%) with thromboembolic episodes (3 deep venous thromboses, one with a pulmonary embolus and sudural hematoma). In this challenging population, local implantable chemotherapy appears relatively safe and a reasonable consideration as a surgical adjunct.

MLTI-12. TIMING OF SYSTEMIC THERAPY ADMINISTRATION RELATIVE TO STEREOTACTIC RADIOSURGERY AND DEVELOPMENT OF RADIATION NECROSIS IN PATIENTS WITH BRAIN METASTASES

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PURPOSE: The mainstay of oncologic therapy for patients with brain metastases involves brain-directed radiation, increasingly given via stereotactic radiosurgery (SRS), and systemic therapy for extracranial disease control. We sought to investigate the association between the timing of systemic therapy and SRS administration on development of radiation necrosis among patients with brain metastases. METHODS: We retrospectively identified 429 patients treated at Brigham and Women's Hospital/Dana-Farber Cancer Institute with SRS for newly-diagnosed brain metastases between 2001–2015. Systemic therapy was tiered into 4 categories: chemotherapy, immunotherapy, hormonal therapy, and targeted therapy. All images were manually reviewed by two radiation oncologists specializing in brain tumors to assess the presence versus absence of radiographic necrosis. Patients with radiographic necrosis who harbored associated neurologic symptoms or were managed with steroids/bevacizumab/resection were considered to have symptomatic radiation necrosis. Data were analyzed using univariable Cox regression in SAS v9.4. The median follow-up in surviving patients was 1.79 years. RESULTS: In total, 252/429 and 361/429 patients received systemic therapy pre and/or post SRS, respectively. Patients receiving systemic therapy ≤5 days before SRS displayed higher rates of radiographic (HR 2.48, 95% CI 1.06–5.81, p=.04) and symptomatic (HR 3.74, 95% CI 1.08–12.98, p=.04) necrosis; a similar association was seen in patients receiving systemic therapy ≤5 days after SRS (HR 1.72, 95% CI 0.84–3.53, p=.14 and HR 4.42, 95% CI 1.75–11.14, p=.002, respectively). Trends towards increased necrosis risk were noted when comparing systemic therapy administration 1–5 days versus 6–10 days before/after SRS. The above 4 associations were significant when restricting the cohort to patients receiving targeted systemic therapy (HR-range 3.57–21.49, p-range 0.01–0.04). CONCLUSIONS: Our results suggest that a reasonable delay between SRS and systemic therapy administration may reduce rates of radiation necrosis, even among patients receiving targeted therapies. Validation in an independent data set would lend further support to this concept.

MLTI-13. RESPONSE ASSESSMENT OF MELANOMA BRAIN METASTASES TREATED BY STEREOTACTIC RADIOTHERAPY OR IMMUNOTHERAPY OR BOTH: A COMPARISON OF RECIST 1.1, RANO AND IRANO CRITERIA

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BACKGROUND: The evaluation of response for brain metastases (BM) may be challenging in the context of treatment by stereotactic radiotherapy (SRT) or immunotherapy or both. METHODS: We reviewed clinical and neuroimaging data of 62 melanoma patients with newly diagnosed BM treated by the combination of immunotherapy and SRT (n=33, group A), immunotherapy alone (n=10, group B) or SRT alone or in combination with other systemic therapies (n=19, group C). Response was assessed using RECIST 1.1, RANO or iRANO criteria. RESULTS: BRAF mutations were noted in 26 patients. 54 patients (87%) had 1–3 metastases. The median DS-GPA was 3. After a median follow-up of 30.5 months, 39 patients have experienced CNS progression, 16 (48.5%) in group A, 9 (90%) in group B, 14 (73.5%) in group C. Median PFS was 129.5 days (range 82–532) in group A, 75 days (range 35–203) in group B, 136 days (range 59–514) in group C. Forty-seven patients (76%) had died at the time of the analysis, 22 (66.5%) in group A, 7 (70%) in group B, 18 (94.5%) in group C. Median OS was 345 days (range 65–1824) in group A, 174.5 days (range 50–1361) in group B, 409 days (range 102–1244) in group C. 52 MRI scans were available for central review: pseudoprogression was documented in 9 patients (29%) in group A, 0 (0%) in group B, 5 (29.5%) in group C. Response rates were similar with all three sets of response criteria. Progressive disease was less often called when applying iRANO to assess SRT target lesions. CONCLUSIONS: Despite the retrospective nature and the small sample size, these data may indicate that the omission of SRT from first-line treatment may compromise outcome. Pseudoprogression is uncommon with immunotherapy alone; pseudoprogression rates were similar after SRT alone or in combination with immunotherapy or other systemic treatment.

MLTI-14. A SYSTEMATIC REVIEW OF TREATMENT PARADIGMS FOR PATIENTS WITH BREAST CANCER AND ONE OR MORE BRAIN METASTASES

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BACKGROUND: Upwards of 50% of patients with advanced breast cancer are diagnosed with brain metastases (BM). Treatment options for these patients have been rapidly evolving due to increased understanding of the tumor pathophysiology and its genetic underpinnings. This systematic review of randomized controlled trials (RCTs) aims to clarify the evidence guiding the treatment of brain metastases from breast cancer. METHODS: MEDLINE, EMBASE, Cochrane Controlled Register of Trials, ClincialTrials.gov, and Web of Science were searched from inception to October 2018 for RCTs comparing treatments for breast cancer BM. We screened studies, extracted data, and assessed risk of bias independently and in duplicate. Outcomes assessed were overall survival (OS), progression-free survival (PFS), and adverse events (Grade 3+). RESULTS: Among 3188 abstracts, only 3 RCTs (N=412; mean sample size per group N=54.7) meeting inclusion criteria were identified. The studies were phase II or III open-label parallel superiority trials. Inclusion criteria among these trials consisted of age >18 with radiologic evidence of >1 BM. Exclusion criteria consisted of poor-performance functional status (ECOG >2 or KPS < 70). The treatment groups included whole-brain radiation therapy (WBRT) vs WBRT + Temozolomide, WBRT vs WBRT + Efaproxiral, and Afatinib vs Vinorelbine vs investigators' choice (86% of these patients received WBRT or SRS prior to study enrolment). While two trials found no significant difference in OS, one trial found significant improvement in OS with Efaproxiral in addition to WBRT compared to WBRT alone (HR 0.52; 95%CI 0.332–0.816). No significant differences were found with PFS or rate of adverse events amongst treatment groups. CONCLUSION: Considering the high prevalence of breast cancer BM and our improved understanding of genomic/molecular features of these tumors, a greater number of RCTs dedicated at this disease are needed.

MLTI-15. A CASE SERIES OF PRE-OPERATIVE GAMMA-KNIFE RADIOSURGERY FOR RESECTABLE BRAIN METASTASES

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Recent advances in the systemic treatment of various cancers have resulted in longer survival and higher incidence of brain metastases. Phase 3 trials in north America and in Japan have demonstrated that stereotactic radiosurgery will be a standard adjuvant modality following surgery for resectable brain metastases. However, we don't know the optimal sequence of this combination therapy. We hypothesized that pre-operative stereotactic radiosurgery for resectable brain metastases provides favorable rates of local