fluorothymidine (FLT) is a PET tracer which correlates with cellular proliferation and may improve response assessment. METHODS: A phase I trial of whole brain radiotherapy (WBRT)+sorafenib was conducted using a 3 + 3 design. Sorafenib was given daily at the start of WBRT for 21 days (dose levels: 200mg, 400mg, and 600mg). The primary endpoints were to determine a maximum tolerated dose (MTD) and to evaluate safety and toxicity. The secondary endpoint was CNS progression-free survival (CNS-PFS). Macdonald Criteria were used for response assessment. A correlative serial FLT-PET imaging study was conducted to assess radiographic changes among pts receiving WBRT +/- sorafenib, in parallel with MRI. RESULTS:13 pts in the dose escalation were evaluable for dose-limiting toxicity (DLT). DLTs were: Grade (G) 4 increased lipase at 200mg (1 pt) and G3 rash at 400mg (3 pts) level. MTD was 200mg. Six additional pts were treated in an expansion cohort without additional DLT. 14 pts were evaluable for response. The overall response rate was 71%: 4 complete + 6 partial responses. Median follow up was 14 months (range: 3–44). Median CNS-PFS was 12.8 months (95%CI: 6.7-NR). A total of 15 pts (10 WBRT+sorafenib and 5 WBRT) were enrolled in the FLT-PET study: all had baseline FLT-PET, 14 with follow up at 7–10 days post WBRT (FU1), and 9 with followup at 12 weeks post WBRT (FU2). 55 baseline lesions were observed and analyzed: 38 at FU1 and 15 at FU2. Decline in average SUVmax of ≥25% was seen in 9/10 (90%) of WBRT+sorafenib pts and 2/4 (50%) of WBRT only pts at FU1. CONCLUSIONS: Concurrent WBRT+sorafenib appears safe at 200mg daily dose with clinical activity. This combination should be considered for further efficacy evaluation. NCT01724606 and NCT01621906.

MLTI-03. FIRST-LINE STEREOTACTIC RADIOSURGERY COMBINED WITH SYSTEMIC TARGETED AND IMMUNE CHECKPOINT INHIBITOR THERAPY IN MELANOMA PATIENTS WITH NEWLY DIAGNOSED BRAIN METASTASES

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BACKGROUND: Of solid tumors, melanoma has the highest propensity for CNS spread with historic median survivals of 5–8 months following brain metastasis diagnosis. We evaluated the impact of systemic BRAF targeted and immune checkpoint inhibitor (ICI) therapies on survival outcomes in patients receiving stereotactic radiosurgery (SRS) for melanoma brain metastases (MBM) and assessed patient treatment burden associated with prolonged survival. METHODS: We retrospectively reviewed the demographics, disease characteristics, therapeutic regimens, overall survival, and first-year cumulative incidence of comorbid disease for patients with de novo MBM treated between 2013 and 2017 at a major melanoma referral center. RESULTS: Among 123 newly diagnosed MBM patients: 65% were male, 24% were 50 years old or less, 50% were BRAF mutated, 63% had multiple intracranial lesions at diagnosis. Locally, 73% received SRS as first-line treatment. Systemically, 73% received ICI, 46% received BRAF targeted therapy, and 12% received neither. With a median follow up of 11 months (mo), total cohort median OS was 13.2 mo. Median OS for first-line SRS combined with ICI and BRAF targeted therapy was 31.0 mo (47% 3-year OS), 17.5 mo (31% 3-year OS) with ICI monotherapy, and 6.1 mo (22% 3-yr OS) alone. SRS and BRAF targeted therapy were associated with improved OS. At one-year follow-up, comorbid conditions with the greatest cumulative incidence were fatigue, nausea, intracranial hemorrhage, deep vein thrombosis, major depressive disorder, and pneumonia. Patients averaged one inpatient visit every 4.5 mo (1 week average length of stay), and 2 advanced imaging studies (MR/CT/PET-CT) per month following MBM diagnosis. CONCLUSIONS: In one of the largest reported MBM series, survival has improved markedly for patients receiving first-line SRS combined with targeted and immunotherapies. Simultaneously, longer life expectancy comes with increasing incidences of comorbid conditions reflecting an evolving complexity of and need for coordination of care for patients with MBM.

MLTI-04. EVOLUTION OF TREATMENT PARADIGMS FOR PATIENTS WITH ≥1 BRAIN METASTASES FROM PRIMARY NON-SMALL-CELL LUNG CANCER – A SYSTEMATIC REVIEW

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BACKGROUND: Brain metastases (BM) are common in non-small cell lung cancer (NSCLC), with approximately 10% of patients presenting with BM at the time of diagnosis. The aim of this systematic review was to critically evaluate the evolution of management paradigms for BM from NSCLC. METHODS: We searched MEDLINE, EMBASE, Web of Science, ClinicalTrials.gov, and CENTRAL for randomized controlled trials (RCTs) published until October 2018. Comparative RCTs based on > 50 patients were selected. The primary outcomes of interest were overall survival (OS) and progression-free survival (PFS). RESULTS: Among 3188 abstracts, 14 RCTs (2494 patients) met inclusion criteria. Median sample size was 97 (range 59–538). Most trials were open-label, parallel, superiority trials. All included patients aged >18 with histologically proven NSCLC and >1 BM proven on CT/MRI. The majority of trials (11/14) excluded patients with non-favorable performance status (ECOG, KPS, or WHO scales), prior SRS or WBRT, and/or leptomeningeal metastases. Interventions assessed included WBRT (11/14), SRS (3/14), targeted therapies (e.g. EGFR inhibitors, 5/14), and various chemotherapeutic regimens (12/14). Most trials (12/13) reported no significant difference in OS between interventions. 4/10 trials reported a difference in PFS, two of which only included patients with EGFR-mutant NSCLC; these showed a significant increase in PFS in patients managed with EGFR inhibitors. The other two trials reported longer PFS with sodium glycididazole + WBRT vs. WBRT alone (p=0.038) and temozolomide + SRS vs. SRS alone (p=0.003). The incidence of adverse events was consistent across most treatment groups. CONCLUSIONS: Most trials showed no significant improvement in OS; however, improvement in PFS was seen in several trials, most notably in EGFR-positive patients treated with EGFR inhibitors. Given the long-standing merit of radiation-based therapies for BM management, these data support the need for an in-depth meta-analysis assessing the comparative efficacy of current management paradigms for specific patient populations.

MLTI-05. IDENTIFYING BRAIN METASTATIC CASES FROM FREE TEXT CLINICAL NARRATIVES WITH REFINEMENT OF SEMANTIC HETEROGENEITY USING MACHINE LEARNING

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INTRODUCTION: Brain metastatic disease (BM) is ripe for discovery using computational tools like machine learning (ML) due to disease complexity and multidimensional critical data (imaging, genomics, primary disease, drug exposures)[1]. Leveraging real-world-evidence' (RWE) from routine health data to inform clinical management is hindered by fragmented unstructured data and semantic heterogeneity[2]. Clinical data in EHR and institutional registries are typically free text narratives absent common data elements (CDE). Curating existing data into CDE with machine learning (ML) may inform contemporary approaches (RWE, N-of-1 trials, and precision medicine) that are dependent on large high-quality datasets. Harvesting existing institutional registries may expand demographic representation, confirm benchmarks of established treatments, and provide test environment for prospective ML applications. METHOD: An R-based deep convoluted neural network (DNN) using keras and an API for Tensorflow python was trained on physician narratives of 2000 BM cases and 8000 other CNS conditions labeled by diagnosis spanning 17 years[3,4]. The ML model was tested with 405 non-labeled narratives to: A) Identify BM from other CNS conditions (i.e. glioma, meningioma, non-tumor). B) Evaluate word embedding using GLoVe[5] to standardize abbreviations and misspellings by assigning terms to CDE by training the model to plot "mets", "metastases" and "spine" with the 20 most similar contextual words. RESULTS: DNN architecture achieved 97% accuracy in distinguishing BM (n=178) for others (n=227). "Mets" and "metastasis" have a connected contextual network suggesting shared meaning, whereas spine did not share a network. CONCLUSIONS: ML can identify BM cases in free-text registries which can serve as a quality control measure and aid data aggregation. Standardizing shorthand terminology to CDE with DNN trained in word embedding can possibly address semantic heterogeneity and facilitate data automation. Solutions are needed to compile and automate quality BM data across institutions to achieve the volume and complexity required for contemporary analysis using ML.

MLTI-06. BEVACIZUMAB VERSUS SURGICAL INTERVENTION FOR RADIATION NECROSIS IN PREVIOUSLY IRRADIATED BRAIN METASTASES

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INTRODUCTION: Both medical management with bevacizumab and surgical management via craniotomy or more recently with laser interstitial thermal ablation (LITT) have been shown to be efficacious in the management of radiation necrosis (RN) after radiosurgery for brain metastases (BM). Indications for how to choose medical versus surgical management however remains unclear. METHODS: Single-institution chart review was performed of all patients with biopsy or radiographically confirmed RN after radiosurgery for BM between 2011 and 2017. Progression-free survival (PFS) and overall survival (OS) were compared between those treated using bevacizumab versus surgical intervention. RESULTS: 15 patients underwent craniotomy, 18 patients underwent LITT, and 18 patients were treated with bevacizumab. Those treated with bevacizumab had significantly higher number of re-