CMET-34. IMPROVEMENT OF LEPTOMENINGEAL DISEASE FOLLOWING INFECTIOUS MENINGITIS

Nicholas Metrus, Carolos Kamiya, Shiao-Pei Weathers, Christa Seligman, and Barbara O'Brien; University of Texas MD Anderson Cancer Center, Houston, TX, USA

INTRODUCTION: The incidence of leptomeningeal disease (LMD) is increasing, due to better imaging, earlier diagnosis and improved systemic disease control. However, many of the systemic therapies do not cross the blood brain barrier (BBB) and, despite treatment with radiation and/or intrathecal (IT) chemotherapy, median survival is approximately 4-6months in solid tumors complicated by LMD. Repeated IT injections increase the risk of CNS infection. Preclinical models have shown that infectious meningitis transiently modifies the BBB. METHODS: Our series consisted of 6 LMD patients (5 breast cancer primary, 1 lung cancer primary) treated on IT chemotherapy at MD Anderson Cancer Center between 2013 and 2018, who subsequently developed infectious meningitis. Three patients had history of parenchymal metastases in addition to LMD and four had history of radiation to brain and/or spine. LMD was confirmed by cytology and/or imaging. All were treated with IT topotecan. RESULTS: CSF cultures were positive for *Proprionobacterium acnes* in three patients, *Pseudomonas aeruginosa* in two, and *Raoultella ornithinolytica* in one, who died shortly thereafter. Antibiotic regimens were variable. Three patients went on to receive IT chemotherapy post-infection (two never discontinued IT chemotherapy throughout infection). Those that had IT chemotherapy post-infection cleared CSF and imaging findings of LMD or maintained stability of radiographic LMD burden until death. No patients died directly from LMD. One patient, who developed infection after Ommaya placement and was never initiated on IT chemotherapy, still cleared his CSF of malignant cells. Excluding the patient who died shortly after meningitis diagnosis, the average time from meningitis diagnosis to death was 8.8 months and the average median survival from LMD diagnosis to death was 14 months. CONCLUSION: Our findings support further evaluating the safety and timing of IT chemotherapy with active infectious meningitis and the potential synergistic benefit of increased immunogenicity and chemotherapy in LMD.

CMET-35. COMPETING RISKS ANALYSIS OF FACTORS INFLUENCING DEVELOPMENT OF LEPTOMENINGEAL METASTASIS IN BREAST CANCER PATIENTS RECEIVING STEREOTACTIC RADIOSURGERY FOR LIMITED BRAIN METASTASES

Michael Zhang[1], Ann Lazar[2], Jason Chan[1], Chelsea Xu[3], August Anderson[1], Javier Villanueva-Meyer[4], Mike McDermott[4], Michelle Melisko[5], Patricia Sneed[4], Olivier Morin[1], and Steve Braunstein[4]; [1]Department of Radiation Oncology, University of California, San Francisco, San Francisco, CA, USA, [2]Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA, [3]Department of Medicine, University of California, San Francisco, San Francisco, CA, USA, [4]University of California, San Francisco, San Francisco, CA, USA, [5]Department of Medicine, Division of Hematology/Oncology, University of California, San Francisco, San Francisco, CA, USA

Leptomeningeal metastasis (LM) is a late stage manifestation of advanced breast cancer frequently managed with whole brain radiotherapy (WBRT) and/or intrathecal chemotherapy. A subset of breast cancer patients who undergo stereotactic radiosurgery (SRS) for limited brain metastases (BM) ultimately develop LM. We hypothesized that this subset of high-risk patients may be identified by patient, disease, and/or treatment parameters. Clinical records from 133 breast cancer patients from a single institution who underwent SRS for BM between February 2010 and March 2018 were retrospectively analyzed. Variables including histopathology, BM features, systemic disease burden, and prior treatments were analyzed. Cumulative incidence rates were estimated with death as a competing risk. Dichotomous variable cutoffs were based on the 75th percentile value. In our cohort, 27 (20.3%) patients ultimately developed LM. With a median follow up of 21.2 months after diagnosis of BM, the actuarial rate of LM at 24 months was 15.2% (95% CI, 8.7%-21.7%). Median OS after diagnosis of LM was 7.0 (95% CI, 3.1–15.4) months. There was significantly increased risk of LM with ≥9 vs < 9 BM at BM diagnosis (28.1% vs 10.8% [24-month actuarial risk], subdistribution HR 2.4, p=0.027), and ≥11 vs < 11 cumulative number of BM treated (25.7% vs 11.7% [24-month actuarial risk], subdistribution HR 2.7, p=0.01). Variables not significantly associated with the risk of LM included tumor receptor status (ER, PR, HER2, triple negative), graded prognostic assessment, KPS, extracranial metastases, total BM volume, prior WBRT, or prior surgical resection. Time intervals between SRS treatments immediately preceding LM diagnosis was not significantly different from other time intervals. In conclusion, patients with a larger number of brain metastases at BM diagnosis (≥9) or cumulatively treated (≥11) appear to be at higher risk of developing LM and may benefit from stronger consideration of WBRT, intrathecal chemotherapy, and/or brain-penetrating systemic therapy.

CMET-36. IMMUNOTHERAPY VERSUS STANDARD OF CARE IN MELANOMA BRAIN METASTASES WITH KNOWN BRAF STATUS

Addison Barnett[1], Soumya Sagar[1], Adam Lauko[2], Wei (Auston) Wei[3], Samuel Chao[1], David Peereboom[1], Glen Stevens[1], Lilyana Angelov[1], Jennifer Yu[1], Erin Murphy[1], Alireza Mohammadi[1], John Suh[4], Gene Barnett[1], and Manmeet Ahluwalia[5]; [1]Cleveland Clinic, Cleveland, OH, USA, [2]Cleveland Clinic Lerner Research Institute, Cleveland, OH, USA, [3]Taussig Cancer Institute, Cleveland, OH, USA, [4]Cleveland Clinic Foundation, Cleveland, OH, USA, [5]Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA

INTRO/OBJECTIVE: A mutation of the BRAF protein is seen in approximately 50% of melanoma patients. Immune checkpoint inhibitors (ICI) are standard therapy in melanoma patients independent of a patient's BRAF status. The primary objective of this study is to investigate the impact of BRAF status in patients treated with ICI compared to non-ICI systemic therapy on overall survival (OS) in patients with melanoma brain metastasis (MBM). METHODS: We reviewed 351 patients with MBM treated at our tertiary care center between 2000 and 2018. Of these, 144 had known BRAF status, 71 of which were BRAF mutant and 73 were BRAF wild-type. OS was calculated from the date of diagnosis of MBM to compare the efficacy of ICI to other systemic therapies. Many of these patients received multiple lines of treatment including targeted therapies at some point during their care. The log-rank test and Cox proportional hazard model was utilized to determine differences in OS. RESULTS: Eighty-four percent of patients received local therapy that included either surgery, stereotactic radiosurgery, or whole brain radiation therapy. In BRAF wild-type patients, 40 received ICI and 33 underwent non-ICI systemic therapy with a median survival (5.6 vs 7.1 months) and 2-year survival (28% vs 32%), respectively (p=0.64). Of the BRAF mutant patients, 33 received ICI and 38 did not with a median survival (17.1 vs 9.0 months) and 2-year survival (36% and 19%), respectively (p=0.014). When controlling for age, KPS, ECM, and number of lesions, BRAF mutant MBM patients treated with ICI compared to non-ICI had an OS hazard ratio, HR=0.4 (95% CI=0.21 – 0.78, p=0.0069). CONCLUSION: ICI therapy in BRAF mutant MBM patients results in improved OS compared to those with non-ICI systemic therapy. No such difference was observed in the BRAF wild-type cohort.

CMET-37. CLINICAL UTILITY OF ENCYCLOPEDIC TUMOR ANALYSIS TO TREAT PATIENTS WITH BRAIN METASTASIS IN REFRACTORY CANCERS

Timothy Crook[1], Darshana Patil[2], Dadasaheb Akolkar[3], Anantbhushan Ranade[4], Amit Bhatt[4], Vineet Datta[2], Jatinder Bhatia[2], Stefan Schuster[5], Revati Patil[2], Ajay Srinivasan[2], Harjeet Kathuria[2], and Rajan Datar[2]; [1]St. Luke's Cancer Center, Royal Surrey County Hospital, Guildford, England, United Kingdom, [2]Datar Cancer Genetics Limited, Nasik, Maharashtra, India, [3]Datar Cancer Genetics Limited, Nasik, India, [4]Avinash Cancer Clinic, Pune, Maharashtra, India, [5]Datar Cancer Genetics Europe GmbH, Bayreuth, Germany

Brain metastasis in solid organ cancers is associated with adverse prognosis, which is further aggravated by limited systemic treatment options. Such patients are also often excluded from clinical trials since their poor prognosis is perceived to unfavorably impact trial outcomes and misrepresent efficacy data. We retrospectively evaluated the efficacy of treatment guided by Encyclopedic Tumor Analysis (ETA) in patients with advanced refractory malignancies and brain metastases to determine the impact on outcomes. Freshly biopsied tumor tissue (primary / lymph node / liver) and peripheral blood of patients were used for integrational multi-analyte investigations as part of ETA, which included gene mutations, gene expression, and in vitro chemosensitivity profiling of viable tumor cells. Based on ETA, patients received individualized therapy recommendations. All patients underwent a PET-CT scan as well as MRI scan prior to treatment start to determine extent of disease. All patients underwent follow-up PET-CT scans and brain MRI scans every 6–8 weeks. Of the ten patients with brain metastases, which were evaluated after receiving ETA-guided treatment, the median follow-up duration was 97 days (range 79 – 180 days) during which all ten patients remained progression-free. Median time to progression for these patients on the last (failed) line of treatment was 91 days (range 30 - 176 days). Five patients showed partial response and five patients showed stable disease while on ETA-guided treatment. During the follow-up period, all brain metastases were either stable (n=7) or had regressed (n=3), and none of the patients reported new brain lesions. Personalized ETA guided treatments imparted clinical benefit by halting disease progression in this cohort of high-risk patients who would have otherwise been considered for palliative regimens due to perceived unfavorable prognosis.