CONCLUSION: Median overall survival was higher than historical experience in this retrospective analysis. It is CSF CEA level, but not serum CEA level that correlated with prognosis for LM from NSCLC.

LPTO-08. INTRATHECAL TRASTUZUMAB PLUS/MINUS IT TOPOTECAN FOR PATIENTS WITH HER2+ BREAST CANCER AND LEPTOMENINGEAL METASTASIS

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BACKGROUND: Leptomeningeal metastasis (LM) is an aggressive complication of cancer. No standard therapies exist, although at our institution we commonly use IT topotecan in good-risk patients. We report our experience in patients with HER2+ breast cancer (BC) LM treated with intrathecal (IT) trastuzumab +/- IT topotecan. METHODS: We retrospectively reviewed records of patients managed with IT trastuzumab at MD Anderson Cancer Center from 2016–2019. Demographics, clinical course, and outcomes data (Kaplan-Meier) were collected and analyzed. RESULTS: 14 female patients (median age 49, range 33–67) with HER2+ BC (29% hormone receptor (HR) positive, 71% negative) were treated with IT trastuzumab (titrated to 40 mg -100 mg/week); 8 (57%) received concurrent IT topotecan. LM diagnosis was made in 64% by MRI alone, and 36% by both MRI and CSF cytology; 79% had brain metastases (BM), and of those, 55% (6/11) had active BM at LM diagnosis; 57% received WBRT prior to initiation of IT therapy. Median KPS was 90 (range, 60–100). Of those with initially positive cytology, 50% (4/8) converted to negative during treatment. MRI findings improved in 79%; 79% were symptomatic at diagnosis (most commonly ataxia, cranial neuropathy, headache); 70% (7/10) had symptom improvement on IT therapy. The only IT-associated symptom reported was mild nausea that occurred in 29%. Median time from diagnosis of metastatic BC was 10.7 mos. (range 0–83 mos); 36% had active extra-CNS disease and 86% received concurrent systemic therapy; 57% underwent change in systemic therapy during IT treatment; 91% were progression-free at 6 months, 32% at 24 months. Median overall survival from LM diagnosis was 24.7 months (95% CI 10.7, NR). CONCLUSIONS: IT trastuzumab is a safe and promising therapy for patients with HER2+ BC and LM. Dual IT therapy with trastuzumab and topotecan was well-tolerated and warrants further investigation in a larger study.

LPTO-09. INTRATHECAL TOPOTECAN FOR LEPTOMENINGEAL METASTASIS IN SOLID TUMORS: THE MD ANDERSON EXPERIENCE

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BACKGROUND: Leptomeningeal metastasis (LM) is a devastating complication of cancer resulting in progressive neurologic decline. Although intrathecal (IT) methotrexate and cytarabine are commonly used for solid tumor LM, we routinely use IT topotecan due to previously demonstrated similar efficacy and modest side effect profile. We report updated data on our experience. METHODS: We reviewed clinical records of patients with solid tumor LM treated with IT topotecan at MD Anderson Cancer Center from 2008–2018. Patient characteristics and course were summarized by descriptive statistics. Overall survival (OS) was estimated with Kaplan-Meier, and the association of KPS with OS evaluated with log-rank test. RESULTS: 138 patients were treated with IT topotecan. The median age was 54 years (range, 22–76), 81% were female. Breast cancer (62%) was the most common primary, then lung (21%), melanoma (4%). Median time from primary diagnosis to LM was 3.4 (range, 0.07–25.2) years. LM was diagnosed by CSF cytology alone in 8 (6%), MRI alone in 21 (15%), CSF+MRI in 108 (78%). Patients most commonly presented with headache (39%) or sensory changes (18%), and had a median KPS of 80 (range, 60–100). 66% had prior/concurrent brain metastasis. 71 patients (52%) received WBRT following LM diagnosis. 41% had adverse effects, most commonly nausea/vomiting (22%) and headache (20%). The majority were grade 1 (63%); 7 were grade 4 (2 Ommaya malfunctions and 5 infections). Patients received a median of 9 (range, 1–79) doses, most stopped due to CNS progression (42%). Median OS was 6.5 months (95% CI 4.7, 7.8). OS was 3.8 mos with KPS ≤70, vs. 7.5 mos with KPS >70 (p< 0.001). CONCLUSIONS: IT topotecan has a modest side effect profile. Patients with higher functional status at diagnosis had significantly better survival. This study supports the continued use of IT topotecan as a well-tolerated option for LM.

LPTO-10. ASSESSMENT OF LEPTOMENINGEAL CARCINOMATOSIS DIAGNOSIS AND OUTCOMES FROM 2005 TO 2015 AT THE OHIO STATE UNIVERSITY

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BACKGROUND: Leptomeningeal carcinomatosis (LMC) is a complication of solid tumor malignancies where tumors metastasize to the leptomeninges. LMC complicates 4–15% of malignancies with incidence increasing as survival of patients with advanced cancer improves. Diagnostic methods include magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) cytology. We assessed detection methods, incidence, and outcomes of LMC at The Ohio State University Comprehensive Cancer Center from 2005–2015. METHODS: This was a single-institution retrospective study of 160 patients with confirmed diagnosis of LMC. Patients with hematologic and central nervous system malignancies were excluded. Descriptive statistics were used to summarize demographic and clinical characteristics. Overall survival (OS) was defined as time from LMC diagnosis to death or last known follow-up, and was generated using Kaplan-Meier methods. RESULTS: Median age of LMC diagnosis was 55.8 years (range: 48, 62.5). 69 (43%) patients had primary breast cancer, 41 (26%) had lung cancer, and 17 (11%) had melanoma. 73 patients (46%) presented with stage IV disease at initial diagnosis of the primary cancer, 41 (26%) with stage III disease, and 26 (16%) with stage II disease. Median time from diagnosis of primary cancer to diagnosis of LMC was 2 years (range: 0, 31.2). 158 (99%) patients had metastases at the time of LMC diagnosis, predominantly in bone (36%) or brain (36%). Median OS was 1.9 months (CI: 1.3, 2.5). 160 (100%) patients had an MRI of the brain or spine and 155 (97%) had MRI findings consistent with LMC. 75 (47%) patients underwent lumbar puncture, and 39 (52%) had CSF cytology positive for malignancy. CONCLUSIONS: Despite treatment, prognosis remains poor and confirmation of diagnosis can be challenging. This study highlights the need for novel therapeutics and improved diagnostic techniques for patients with LMC.

CLINICAL TRIALS

TRLS-01. RADIOSURGERY FOLLOWED BY TUMOR TREATING FIELDS (TTFIELDS) FOR BRAIN METASTASES (1–10) FROM NSCLC IN THE PHASE 3 METIS TRIAL

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Tumor Treating Fields (TTFields) are non-invasive, loco-regional, antimitotic treatment comprising alternating electric fields that have demonstrated efficacy in preclinical non-small cell lung cancer (NSCLC) models. TTFields to the brain was safe and extended overall survival in newly-diagnosed glioblastoma. The METIS study [NCT02831959] investigates the efficacy and safety of TTFields in NSCLC patients with brain metastases. NSCLC patients (N=270) with 1–10 brain metastases are randomized 1:1 to stereotactic radio surgery (SRS) followed by continuous TTFields ((150 kHz, > 18 hours/day) within 7 days of SRS or supportive care. The TTFields portable device delivers TTFields to the brain using 4 transducer arrays, while patients receive the best standard-of-care for their systemic disease. Patients are followed every two months until second intracranial progression. Key inclusion criteria: KPS ≥70, new diagnosis of 1 inoperable or 2–10 supra- and/or infratentorial brain metastases from NSCLC amenable to SRS; KPS ≥70; and optimal therapy for extracranial disease. Prior WBRT or surgical resection of metastases, a single resectable lesion or recurrent brain metastases were exclusionary. Primary endpoint was time to 1st intracranial progression. Secondary endpoints included time to neurocognitive failure (HVLT, COWAT and TMT), overall survival, radiological response rate (RANO-BM and RECIST V1.1); quality-of-life; adverse events; time to first/second intracranial progression for patients with 1–4 and 5–10 brain metastases; bi-monthly intracranial progression rate from 2–12 months; and time to second intracranial and distant progression. The sample size (N=270) was calculated using a log-rank test (Lakatos 1988 and 2002) with 80% power at a two sided alpha of 0.05 to detect a hazard ratio of 0.57. In August 2018, an independent Data Monitoring Committee (DMC) performed a review of the METIS trial data collected to that point. The DMC concluded that no unexpected safety issues have emerged on the study, and recommended to continue the METIS study as planned.