spective evaluation suggest olaparib in combination with radiotherapy +/- bevacizumab is well tolerated and can provide additional benefit in patients with brain metastases secondary to ovarian carcinoma.

MULTIMODALITY

MLTI-01. STUDY ON THE ASSOCIATION BETWEEN PRONE LOCATIONS AND PROGNOSIS OF BREAST CANCER BRAIN METASTASES VIA VOXEL ANALYSIS

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PURPOSE: This study aimed to analyze the preferred locations of secondary brain tumors of breast carcinoma according to different biological characteristics. METHOD: 161 Breast cancer brain metastasis (BCBM) patients diagnosed between January 2007 and February 2018 were retrospectively analyzed. MR images when brain metastases occurred were collected, registered, segmented. The frequency and p-value heatmaps were constructed to compare two biological phenotypes using two-tailed Fisher's exact test. Age, treatments, the status of ER, PR, and HER2, luminal subtype, tumor marker levels in peripheral blood including CEA, CA19-9, and CA15-3 were statistically analyzed. Survival data were analyzed by Kaplan–Meier method, log-rank test, and multivariate logistic regression. RESULT: The frequency heat map shows lesions of patients with BCBM are more inclined to the cerebellar hemisphere. Older patients(>49 years old, median age) mainly occur in the left frontal lobe, the right parietal lobe, and adjacent meninges comparing with white matter of the left parietal lobe, cerebellar vermis, and areas around the fourth ventricle among younger patients and the difference is significant. Patients with tumors located on the surface of the brain are more likely to undergo surgical treatment, however, conservative treatment was considered if metastases are located at the midline structure. ER and PR-positive and HER-2 enriched patients have more significance in metastases, at the left parieto-occipital junction area, frontal lobe, parietal lobe, cerebellar hemisphere, and adjacent meninges. Metastases with high levels of CEA are found significantly at areas around the central anterior gyrus. Lesions with an elevated level of CA19-9 and CA15-3 tend to be frontal, parietal, and occipital. Besides, HER-2 enriched in primary sites and a normal level of CA15-3 in peripheral blood were two independent protective factors in determining prognostic outcomes. CONCLUSION: The preferred locations of BCBM could be clues of further study and helpful for clinical strategies.

MLTI-02. IMPACT OF DRIVER MUTATIONS ON TIMING, PATTERN, TREATMENT, AND OUTCOME IN PATIENTS WITH BRAIN METASTASES FROM NON-SMALL CELL LUNG CANCER

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OBJECTIVE: To assess the impact of driver mutations in non-small cell lung cancer (NSCLC) on the formation and treatment outcome of brain metastases (BM). PATIENTS AND METHODS: We retrospectively analyzed patients with BM from NSCLC with respect to driver mutations and assessed timing and pattern of BM development as well as local cerebral control and survival after BM treatment. RESULTS: We included 253 patients. Histology was adenocarcinoma in 223, squamous cell carcinoma in 25 and not otherwise specified (NOS) in five patients. All tumors were analyzed for known alterations in NSCLC by panel sequencing and fluorescence in situ hybridization (FISH). An activating *KRAS* mutation (n=85) was the most prevalent mutation, followed by activating EGFR mutation (n=31) and *MET* amplification (n=29). Other mutations were detected in 27 patients. No alterations were found in 102 patients. Time to BM development did not differ between the molecular groups (p=.22), nor did the number (p=.72) or location (supra- vs. infratentorial; p=.76) of the BM. Patients underwent multimodal cerebral treatment comprising surgery followed by radiotherapy and/or stereotactic radiosurgery (n=138), whole brain radiotherapy (n=13) or stereotactic radiosurgery alone (n=102). Systemic treatment was initiated or continued after BM therapy in 169 patients and its frequency did not differ significantly between genotypes (p=.08) while the modality of medical treatment depended on genotype (p<0.0001). The latter showed longer local cerebral control rates compared to other mutations (0.23) and a longer overall survival compared to *KRAS* and wild type genotypes (p=.015). Systemic treatment (HR 2.1 95%CI 1.4–3.0; p<.0001) and a good clinical status (HR 2.1 95%CI 1.2–3.7; p=0.014) were the only independent factors for further survival. CONCLUSION: The actual known driver mutations do not influence BM formation. Specific genotypes show a better oncological course, presumably due to available molecular treatment.

MLTI-03. THE RELEVANCE OF THE COUNT OF BRAIN METASTASES FOR TREATMENT AND OUTCOME IN NSCLC

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BACKGROUND AND PURPOSE: While data reporting the number of brain metastasis as a prognostic factor for patients with NSCLC, we analyzed whether the prognostic importance of the mere count of brain metastasis in a modern, multimodal treatment setting. PATIENTS AND METHODS: We retrospectively analyzed patients treated for BM from non-small lung cancer between 2010 and 2020. Demographics, baseline characteristics, and tumor-associated parameters were retrieved from an electronic database. Prognostic factors for local cerebral control and survival were identified using the log-rank test and Cox regression analysis. RESULTS: We included 343 consecutive patients (male n=187, female n=156; median age 61 years). Histological subtypes were adenocarcinoma (n=283), squamous-cell carcinoma (n=42) and neuroendocrine carcinoma (n=18). The median number of BM was one (range 1–20). Single (n = 189), oligo (n=110) and multiple BM (n=44) showed in total a median follow up of 10 months (minimum 1, maximum 142). Treatment comprised surgical resection (n=218) with radiotherapy, stereotactic radiosurgery (n=125) and adjuvant systemic therapy (n=203). The median local cerebral control was 11 months (95%CI 8.5 – 13.5) and the median overall survival was 16 months (95%CI 12.8 – 19.2). The number of BM did not influence local control and overall survival rates (p = 0.234 and p = 0.210, respectively). Controlled systemic disease (HR 0.42; 95% CI 0.2284–0.633; p<0.0001), clinical status (Karnofsky Performance Score > 70; HR 0.41; 95% CI 0.265–0.661; p<0.0001) and adjuvant systemic therapy (HR 0.38; 95% CI 0.279–0.530; p<0.0001) were independent prognostic factors for survival. CONCLUSIONS: The mere number of brain metastases is not a prognostic factor for survival and local cerebral control in a multimodal treatment setting.

MLTI-04. THE ROLE OF THE OUTPATIENT REGISTERED NURSE IN THE CARE OF BRAIN METASTASES

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INTRODUCTION: Brain metastases is a complex disease, requiring a skilled clinical team to deliver medical and surgical care. The nurse is an integral member of the interdisciplinary team. Despite this, the role of the nurse in brain metastasis care has been neglected in the literature. Moreover, while education for neurology nursing exists, there is a paucity of literature defining the nursing care specific to brain metastases. The aim of this study was to describe the essential nursing functions in brain metastases within medical and surgical clinics. METHODS: A working-group comprised of 2 registered nurses and a clinical nurse specialist in specialty brain metastases at Memorial Sloan-Kettering Cancer Center was formed. A KSA framework was used to develop a survey to assess nurses' knowledge, skills, and attitudes regarding care of patients with brain metastases. 2 nurses were surveyed. Oncology nursing competencies were scored by medicine and surgical nurses for importance. Mean scores were calculated and ranked. RESULTS: Nurses consistently reported care coordination; symptom management and monitoring parameters; knowledge of treatment modalities; and referrals as key competencies. More variably endorsed competencies included access devices (implanted port and Omaya); managing immunocompromised patients; and legal issues (consent). The nurses reported important knowledge includes screening and treatment guidelines; epidemiology; disease states including brain metastases and leptomeningeal disease; and tumor histology. Important skills include neurological exam; triage; critical thinking; and patient education. Important attitudes include being empathetic, communicative, positive, truthful, and realistic. CONCLUSION: As the care of the patient with brain metastases evolves, interdisciplinary clinical practice models with advanced nursing training must occur. As the repertoire of clinical trials for patients with brain metastases continues to expand, future studies should assess the effects of specialized nursing training on clinical outcomes in patients with brain metastases.

MLTI-05. ADJUVANT RE-IRRADIATION IMPROVES LOCAL CONTROL OF SURGICALLY RESECTED RECURRENT BRAIN METASTASES

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BACKGROUND: The efficacy of salvage resection (SR) of recurrent brain metastases (BrM) post-stereotactic radiosurgery (SRS) is not well described. We sought to characterize the impact of adjuvant post-salvage radiation therapy (PSRT) in this setting and identify tumor-specific variables that influence local control. METHODS: Retrospective analysis of post-SRS recurrent BrM that underwent SR between 2003–2020 at Memorial Sloan Kettering Cancer Center was performed. Cases with histologically-viable malignancy were included and stratified by receipt of adjuvant PSRT within 60 days of SR (PSRT cohort) vs. observation (observation cohort). Resection-site outcomes were described using cumulative incidences and univariate and multivariate competing risks regression accounting for clustering. RESULTS: One-hundred fifty-five recurrent BrM in 135 patients were included. Thirty-nine (25.2%) of the post-operative cavities were treated with adjuvant PSRT, and the remaining 116 (74.8%) cavities were initially observed. Gross- or near-total resection was associated with significantly improved local control compared to subtotal resection (p=0.007). Adjuvant PSRT was associated with a reduced rate of LR at 6 months [18.0% (95%CI: 9.8–33.1%) vs. 35.9% (95%CI: 27.9–46.2%) with initial observation] and 12 months [28.8% (95%CI: 17.0–48.8%) vs. 43.9% (95%CI: 36.2–53.4%)]. On multivariate analysis, adjuvant PSRT (p=0.095), low tumor-viability within the resected BrM (p=0.17), and first-time resection (p=0.035) all independently trended towards improved local control. BrM size at SR (≥3cm vs. <3cm, p=0.48), primary malignancy (p=0.35), and specific PSRT modality (whole or partial brain radiation vs. SRS, p=0.43) were not associated with differences in LR rate. Radiation necrosis (RN) was significantly increased in the PSRT cohort (HR 4.55, 95%CI: 1.26–16.39, p=0.02), though the total percentage with symptomatic RN remained low (PSRT cohort 5.1% vs observation cohort 0.9%). CONCLUSIONS: Local control after SR of a recurrent BrM may be optimized with gross- or near-total resection and adjuvant post-operative re-irradiation, with low symptomatic RN.

MLTI-06. SURGICAL RESECTION PLUS STEREOTACTIC RADIOSURGERY VERSUS SRS ALONE FOR LARGE BRAIN METASTASES: A COMPARATIVE STUDY

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PURPOSE: Large brain metastases (BRM) are challenging to manage. Therapeutic options include Stereotactic Radiosurgery (SRS) or surgery (S) with adjuvant SRS. We sought to compare overall survival (OS), radionecrosis (RN), local failure (LF), pachymeningeal (PMD) and leptomeningeal (LMD) disease in patients treated with SRS vs. S+SRS. METHODS: We reviewed a prospective registry database from 2009 to 2020 and identified all patients with BRM (≥4cc in volume) treated with SRS or S+SRS. WBRT or SRS re-targeting the index lesion were censoring events. Survival percentages were calculated using the Kaplan-Meier method. Differences between groups were tested using the Cox proportional hazards model. RESULTS: 383 patients were identified, 128 and 255 were treated with S+SRS and SRS, respectively. Median ages in the S+SRS and SRS groups were 62.2 (23.6–98.5) and 60.2 (20.2–97.4) (P 0.33). OS at 12 and 24 months was 69% and 41% vs 55% and 20% for the S+SRS and SRS groups, respectively hazard ratio (HR) 1.64 (1.23–2.18) (P<0.001). LF requiring salvage surgery at 12 and 24 months were 3% and 5% vs 8% and 10% for S+SRS and SRS groups, respectively (P 0.067). RN at 12 and 24 months were 9% and 17% vs 15% and 21% for S+SRS and SRS groups, respectively 1.32 HR (0.77–2.29) (P =0.32). PMD disease at 12 and 24 months were 16% and 21% vs 3% and 7% for S+SRS and SRS groups, respectively HR 0.26(0.12–0.56) (P < 0.001). LMD at 12 and 24 months were 4% and 6% vs 2% and 4% for S+SRS and SRS groups, respectively HR 0.73(0.25–2.17) (P 0.57). CONCLUSION: Surgical resection plus SRS correlated with improved OS and a trend towards a decreased incidence of LF compared to SRS alone. However, patients treated with S experienced an increased incidence of PMD.

OTHER

OTHR-01. UNMET CLINICAL NEEDS IN PATIENTS WITH BRAIN METASTASES IN THE CURRENT TREATMENT ERA

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INTRODUCTION: Brain metastases are associated with high morbidity and mortality. With the implementation of effective treatments, long-term survival is possible for some patients. However, most patients still die of their disease. The uncertain prognosis and potentially high symptom burden make managing these patients complex. We aimed to identify the unmet needs in the care of patients with brain metastases. METHOD: Consecutive patients with melanoma or NSCLC brain metastases completed questionnaires assessing distress (distress thermometer), quality-of-life (FACT-general), and information provided on potential symptoms, supportive care, and do-not-resuscitate code (study-specific questionnaire) between Nov'18-Nov'19. Separate focus groups were organized with patients with melanoma brain metastases, primary caregivers of deceased patients, and general practitioners. The results were discussed with hospital-based healthcare professionals to identify additional issues. RESULTS: Questionnaires were completed by 59 patients (25 melanoma, 34 NSCLC) at a median time after brain metastases diagnosis of 11.5 months (range: 0.7–88). Thirty-five patients (59%) experienced distress (distress thermometer ≥4), and 20 patients (34%) expressed interest in supportive care. Furthermore, 40 patients (68%) remembered being informed about potential brain metastases symptoms, and 18 patients (31%) would have liked more information on potential symptoms. Psychosocial support was offered to 31 patients (53%) and 17/51 primary caregivers (33%). Patients emphasized that, despite potential information overload, they preferred to be fully informed about potential symptoms, treatments including outcomes, and psychosocial support availability. Caregivers highlighted the caregiver burden and importance of advance care planning. General practitioners were keen for guidelines on brain metastases symptom management in the home setting. Hospital-based professionals advocated a structured approach, with early identification of palliative care needs and an overview of involved healthcare professionals. CONCLUSION: Our results highlight the need for structured, multidisciplinary management of patients with brain metastases with special attention to symptom and caregiver burden, information provision, and advance care planning.

OTHR-02. ENGINEERED "OF THE SHELF" ALLOGENEIC CELLULAR THERAPIES FOR METASTATIC BRAIN TUMORS

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Brain metastatic patients have multiple metastatic lesions or diagnostically challenging asymptomatic lesions, making surgery an inadequate therapeutic option. Given the challenges related to systemic delivery of a majority of therapeutic agents across the BBB, engineered cell based therapies offer an excellent platform to target metastatic tumors in the brain. We have established the use tumor cell surface receptor targeted allogeneic "off the shelf" gene engineered cellular therapies and developed two different approaches to treat brain metastases. In one approach, we have armed allogenic stem cells (SC) with oncolytic herpes virus (oHSV) variants and tested them in different mouse models of brain metastatic (BM) tumor derived from brain seeking metastatic melanoma tumor cells from patients. We show that intracarotid artery administration of SC-oHSV effectively tracks metastatic tumor lesions and significantly prolongs the survival of brain tumor bearing mice. We also show that a combination of SC-oHSV and PD-L1 blockade increases IFNγ-producing CD8+ tumor-infiltrating T lymphocytes and results in a profound extension of the median survival in syngeneic brain metastatic melanoma mouse models. In another approach, we have explored the versatility of cell mediated bi-functional EGFR and DR4/5-targeted treatment in basal like breast cancer (BLBC) mouse models featuring different patterns of brain metastasis. Most BLBC lines demonstrated a high sensitivity to EGFR and DR4/5 bi-targeting therapeutic protein, EVDRL [anti-EGFR VHH (EV) fused to DR ligand (DRL)]. Functional analyses using inhibitors and CRISPR-Cas9 knockouts revealed that the EV domain facilitated in augmenting DR4/5-DRL binding and enhancing DRL-induced apoptosis. EVDRL releasing allogeneic SCs alleviated tumor-burden and significantly increased survival in mouse models of residual-tumor after macrometastasis resection, perivascular niche micrometastasis, and leptomeningeal metastasis. These findings provide a clinically applicable therapeutic platform to target disseminated metastatic lesions in the brain and define a new paradigm for treatment of brain metastases.

OTHR-03. BRAIN METASTASIS AMONG OVARIAN CANCER PATIENTS

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BACKGROUND: Brain metastasis (BM) are uncommon among ovarian cancer (OC) patients. Their frequency, risk factors and clinical repercussions are not well described. We assessed OC patients who developed BM, the role of BRCA status and survival implications. METHODS: Study cohort included OC patients treated at our center, from 2002–2020. We retrospectively evaluated clinical parameters, risk for BM development and association with survival data. RESULTS: Among 972 OC patients, 28 (2.9%) were diagnosed with BM. Comparing the BM to non-BM group, median age of 60 across both groups, stage III-IV at diagnosis was more common among BM group (96.4% vs. 84.8%, p=0.0065) while platinum sensitivity was similar