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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-visibility 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 (≥ 3 cm vs. < 3 cm, $p=0.48$), 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 (≥ 4 cc 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 allogeneic 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 IFN γ -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