exomes between primary and metastatic sites including the brain. RESULTS: 281 extensive-stage patients and 40 limited-stage patients were included. 12% (30/281) of the extensive-stage patients and 25% (10/40) of limited-stage patients had isolated brain metastases. Patients with limited-stage disease who developed isolated brain metastases had significantly improved mOS as compared to those who developed other sites of metastasis (OS = 38.7 months vs. 20.2 months, p=0.033). Furthermore, mPFS for limited-stage patients with isolated brain metastases was improved compared to other patterns of metastases (PFS = 17.9 months vs. 10.1 months, p = 0.03). NGS demonstrated that NOTCH1 mutations were infrequent in biopsies from all metastatic sites but were common in primary lung tumors. CONCLUSION: In our single center review, patients with limited-stage SCLC who recurred only in the brain had improved survival as compared to those who had other patterns of metastases. Our initial work demonstrates differences in oncogenic gene mutations between the metastatic and primary tumors.

OTHR-16. MOLECULAR PROFILING USING THE 92-GENE ASSAY FOR TUMOR CLASSIFICATION OF BRAIN METASTASES

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BACKGROUND: Nearly 200,000 patients are diagnosed with brain metastases in the US annually. Advances in targeted therapies make definitive diagnosis of the primary tumor type important but can be challenging in many patients. The 92-gene assay is a validated gene expression classifier of 50 tumor types for patients with uncertain tissue of origin diagnoses. Results from a clinical series of brain biopsies and potential impact on treatment were evaluated. METHODS: An IRB approved, de-identified database of clinical and molecular information from biopsies (N = 24,486) submitted for testing with the 92-gene assay (CancerTYPE ID, Biotheranostics, Inc.) as part of routine care were reviewed. Descriptive analysis included patient demographics and molecular diagnoses. RESULTS: Analysis included 464 brain biopsies. A molecular diagnosis was provided in 433 (93.3%) tested (< 5% assay failure rate) with 24 different tumor types. Six primary tumor types made up the majority (67.4%) with almost one-third of the molecular predictions being Lung (31.2%), followed by Neuroendocrine (NET) (9.9%), Sarcoma (7.9%), Skin (6.4%), Gastroesophageal (6.2%), and Urinary bladder (5.8%). All of these 6 tumor types, for which activity in the CNS has been documented, have immune checkpoint inhibitors or other targeted therapies approved in selected cases by the US Federal Drug Administration (FDA). CONCLUSIONS: Molecular classification of brain metastases can identify distinct tumor types for which there are FDA approved targeted medications. Improving diagnostic precision with the 92-gene assay helps identify a subset of therapy-responsive metastatic brain tumors, thus improving therapy and possibly providing better outcomes and survival.

OTHR-17. PHYLOGENETIC RESOLUTION OF TISSUE-SPECIFIC METASTOGENIC CLONES IN RENAL CELL CARCINOMA

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Genomic factors predictive of organ-specific tropism have been established in several models of cancer. However, the evolutionary dynamics at work in metastatic carcinoma have yet to be characterized in detail. We identified a cohort of clear cell renal cell carcinoma (RCC) patients who also had multiple metastasectomies, and performed deep sequencing and statistical inference of subclonal populations to infer phylogeny and essential genetic features acquired prior to systemic dissemination and site-specific colonization. Exome capture and deep sequencing were performed on tissues from 3 patients with polymetastatic RCC (including 12 metastases, multiple regions of primary tumors, and paired germline tissue) to a mean depth of 250x. Somatic point mutations were called with Mutect, and insertions and deletions with Strelka and VarScan. Validation was performed with a custom NimbleGen panel hybridized to a custom sequence library and sequenced to a mean depth of >500x. Allele-specific copy number and clonal prevalence were established using ABSOLUTE, and analyzed with Pyclone across primary and metastatic lesions to determine clonal architecture. Phylogenetic reconstruction identified ancestral clones, with attendant driver mutations in RCC tumor suppressors (including VHL, SETD2, PBRM1, MTOR) and independent subclonal populations in the metastases of all 3 patients. In an index case with multiple metastases separated spatially and temporally, bone and soft tissue metastases demonstrate apparent independent ancestors. Convergent loss of known tumor suppressors was also noted in all cases, and in several cases found in conjunction with de novo mutations in known RCC driver genes acquired late in tumor development. In this demonstration of subclonal and evolutionary analysis of multiple paired multi-organ RCC metastases, we identified subclonal populations characterized by alteration of several tumor suppressors which subsequently exhibited organ-specific patterns of metastasis.

RADIATION

RADI-01. PROGNOSTIC FACTORS OF SHORT SURVIVAL FOR BRAIN METASTASES TREATED WITH SRS WITHOUT WBRT.

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Nowadays multiple brain metastases (up to 10–15 tumors) are treated with SRS alone. The most common diagnosis-specific Graded Prognostic Assessment and Score for Radiosurgery indices are based on data regarding limited brain metastases (1–4). Moreover, many of patients included in that analyses were treated with WBRT or combination of WBRT and SRS and some relevant data were not included due to a retrospective analysis of large datasets. SRS may increase intracranial control of disease, however, treatment of patients with a prognosis of fewer than 3 months survival after SRS may not be clinically reliable. Therefore we conducted an analysis of prospective registry to find the factors that correlate with very short survival after SRS. Materials and methods, A consecutive cohort of 84 patients treated with SRS only for brain metastases between 04.2018-03.2019. Data prospectively collected and introduced into a registry of patients treated with SRS in our department were analyzed. The analyzed factors are age, primary site, histopathology, previous surgery, molecular results, systemic therapy, duration of SRS planning, the extent of extracerebral metastatic disease, number of brain metastases, mass effect and neurological symptoms/ We performed a univariate analysis and multivariate Cox regression model to find a correlation between clinical and molecular data and survival in brain metastases patients treated with SRS only. Factors predicted early death and correlated with survival will be presented at the conference

RADI-02. SINGLE-SESSION VERSUS MULTISESSION GAMMA KNIFE RADIOSURGERY FOR LARGE BRAIN METASTASES FROM NON-SMALL CELL LUNG CANCER: RETROSPECTIVE ANALYSIS

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PURPOSE: To evaluate the efficacy of Gamma Knife radiosurgery (GKS) in patients with large brain metastases by comparing single-session radiosurgery (S-GKS) and multisession radiosurgery (M-GKS), the authors retrospectively analyzed the clinical outcomes of the patients who underwent GKS for brain metastases from non-small cell lung cancer (NSCLC). MATERIALS AND METHODS: Between January 2010 and December 2016, 66 patients with 74 lesions >=10 cm^3 from large brain metastases from only NSCLC were included. Fifty-five patients with 60 lesions were treated with S-GKS; 11 patients with 14 lesions were treated with M-GKS. Median doses were 16 Gy (range, 11–18 Gy) for the S-GKS group and 8 Gy (range, 7–10 Gy) in three fractions for the M-GKS group. RESULTS: With a mean follow-up period of 13.1 months (range, 1.3–76.4 months), the median survival duration was 21.1 months for all patients. Median tumor volume was 14.3 cm^3 (range, 10.0–58.3). The local control rate was 77.0% and the progression-free survival rate was 73.6% at the last follow-up. There were no significant between-group differences in terms of local control rate (p = 0.10). Compared with S-GKS, M-GKS did not differ significantly in radiation-induced complications (38.1% versus 45.4%, p = 0.83). While eight patients who underwent S-GKS experienced major complications of grade >=3, no toxicity was observed in patients treated with M-GKS. CONCLUSIONS: M-GKS may be an effective alternative for large brain metastases from NSCLC. Specifically, severe radiation-induced toxicity (≥ grade 3) did not occur in M-GKS for large-volume metastases. Although the long-term effects and results from larger samples remain unclear, M-GKS may be a suitable palliative treatment to preserve neurological function.

RADI-04. PRETREATMENT VOLUME OF MRI-DETERMINED WHITE MATTER INJURY (WMI) PREDICTS COGNITIVE DECLINE AFTER HIPPOCAMPAL AVOIDANT (HA) WBRT FOR BRAIN METASTASES: SECONDARY ANALYSIS OF NRG ONCOLOGY RTOG 0933

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