melanoma models through modulation of activated T cells and MHC expression in the tumor. Overall, we present the first ever comprehensive single-cell atlas of the tumor microenvironment in melanoma CNS metastases in response to therapy.

LMD-04. FLAIR HYPERINTENSITY ALONG THE BRAINSTEM SURFACE IN LEPTOMENINGEAL METASTASES: A CASE SERIES AND LITERATURE REVIEW

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BACKGROUND: The incidence of leptomeningeal metastasis (LM) is underestimated because of its non-specific signs and the low sensitivity of clinical diagnostic modalities. Cerebrospinal magnetic resonance (MR) imaging with and without contrast enhancement (CE) is a gold standard for the neuroradiological assessment of patients with suspected LM. Previous studies suggested that some LM cases show changes of the brainstem surface on non-contrast MR images without or before the appearance of abnormalities on CE images. We assessed the features of this non-contrast MR finding in a cohort of LM patients in this retrospective single-institution study. METHODS: We reviewed head MR images and clinical data of 142 consecutive patients in whom the final diagnosis was LM. RESULTS: We found that 11 of these 142 patients (7.7%) with LM had band-like hyperintensity on the brainstem surface on non-enhanced FLAIR images, which looked like bloomy rind on cheese. Three of seven patients who were examined using diffusion-weighted imaging showed restricted diffusion in the corresponding lesion site. The above-mentioned 11 patients included 10 women and 1 man, with a median age of 61 years. All 11 patients had primary lung adenocarcinoma. Seven patients had symptomatic hydrocephalus. Ten patients had EGFR-mutated and one had ALK-rearrangement adenocarcinomas. Before the diagnosis of LM, 10 patients had undergone systemic therapy with EGFR-TKI or pemetrexed, and 1 patient with ALK inhibitor and bevacizumab. CONCLUSIONS: We present a series of patients with bloomy rind sign that is non-enhancing LM reliably detected by FLAIR hyperintensity on the brainstem surface. This finding is rare, but may reflect the spread of cancer cells in both the leptomeningeal membrane and the surface of the brain parenchyma specifically in patients with lung adenocarcinomas. Further study is needed to determine the clinical significance of this sign.

LMD-05. PHASE 1B STUDY OF AVELUMAB AND WHOLE BRAIN RADIOTHERAPY (WBRT) IN PATIENTS WITH LEPTOMENINGEAL DISEASE (LMD): PRELIMINARY RESULTS.

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BACKGROUND: LMD has a dismal prognosis with median survivals of 8–10 weeks. Recently the first phase 2 trial of PD-1 inhibitor monotherapy in solid tumor LMD showed median overall survival (OS) 3.6 months. We aimed to determine the safety/efficacy of avelumab with WBRT in patients with LMD from solid malignancies (NCT0371768). This combination can treat tumor directly and increase the permeability of the blood-brain-barrier with increased egress of activated T cells into the meninges/CSF and facilitated Avelumab entry into the CSF. HYPOTHESIS: Combination radioimmunotherapy will produce an activated immunocyte/cytokine profile in CSF. METHODS: Patients received concurrent Avelumab 800mg IV q2weeks x≤5 cycles with WBRT 3000cGy, 10 fractions. Primary endpoints: Safety/DLTs and OS at 3 months. Secondary endpoints: CSF T-cell/cytokine profiles (scRNAseq/phosophoproteomics) and clinical outcomes, to be performed when all 15 patients are accrued to minimize batch effects. RESULTS: Ten patients (5 breast, 4 lung & 1 undifferentiated sinonasal carcinoma) were enrolled (n=8 females, n=2 males, ages 32–79); n=1 patient did not complete WBRT. Patients who received anti-PD-1/PD-1L/PD-L2/CD137/CTLA-4 therapy within 6 months prior to enrollment were excluded. 30% had grade 3 AEs at least possibly related to treatment (n=3 diarrhea, lymphopenia, decreased WBC count). There were no grade 4–5 toxicities. Six patients (66.7%) were alive at 3 months. The estimated median follow up in 9 patients (regardless whether patients failed or not) is 10.49 months (range, 0.95–19.82 months, 95% CI) and the estimated median follow up survival was 19.8 months assessed using the reverse Kaplan-Meier method. Median PFS is 4.27 months (range, 0.30–16.73 months, 95% CI). CONCLUSIONS: In this pilot study, combination of Avelumab and WBRT is safe, and demonstrates encouraging activity in patients with solid tumor LMD. Multiple platform interrogation of CSF may determine mechanisms of LMD therapeutic effects and differentiate responders from non-responders.

LMD-06. A NSCLC PATIENT WITH LEPTOMENINGEAL METASTASIS HARBORING RARE EGFR MUTATIONS G719S AND L861Q BENEFITED FROM DOUBLING DOSAGE OF OSIMERTINIB: A CASE REPORT

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Leptomeningeal metastasis (LM) is a rare but lethal complication of advanced non-small cell lung cancer (NSCLC) that has a devastating impact on patient survival and quality of life. Osimertinib, an irreversible tyrosine kinase inhibitor, is approved as a therapy for advanced NSCLC with epidermal growth factor receptor (EGFR) mutation. However, the efficacy and optimal dosage of osimertinib in the treatment of NSCLC patients with LM who harbor uncommon *EGFR* mutations have yet to be fully investigated. Herein, we report a case of an advanced NSCLC patient with LM carrying *EGFR* G719S and L861Q, who was successfully treated by osimertinib at 160 mg. The patient initially presented with clear cell renal carcinoma and renal metastatic adenocarcinoma, and underwent right nephrectomy. At 2 months after nephrectomy, He developed a disturbance of consciousness and was subsequently diagnosed with NSCLC with LM by meningeal biopsy pathology and cerebrospinal fluid (CSF) cytology. Next-generation sequencing detected the rare *EGFR* mutations G719S and L861R in the meningeal biopsy tissues. The patient was then administered osimertinib at 80 mg quaque die (QD); after 1 month of treatment, his symptoms were alleviated. However, two months later, he experienced epileptic episode. Subsequently, the osimertinib dosage was doubled to 160 mg QD. After 1 month of treatment, the patient achieved central nervous system (CNS) response, and at the time of this manuscript's submission, he had maintained stable disease (SD) for more than 1 year. To our knowledge, this study provides the first clinical evidence that the administration of osimertinib at 160 mg once daily can achieve an encouraging, durable response in an NSCLC patients with LM carrying *EGFR* G719S and L861Q. Aslo, it is recommended to consider performing leptomeningeal biopsy for precision treatment in NSCLC paiernts with leptomeningeal metastasis.

LMD-07. *IN VITRO* AND *IN VIVO* CULTURE OF PATIENT DERIVED-CEREBRAL SPINAL FLUID-CIRCULATING TUMOR CELLS (PD-CSF-CTCS) IN LEPTOMENINGEAL DISEASE (LMD) FROM MELANOMA TO IDENTIFY NOVEL TREATMENT STRATEGIES

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BACKGROUND: Approximately 5% of melanoma patients (pts) will develop LMD. Currently there is no effective treatments for this disease. A significant barrier to the development of effective therapies has been the inability to culture CSF-CTCs for functional analysis. For the first time, we were able to successfully expand CSF-CTCs *in vitro* and *in vivo*. We assessed gene signatures of PD-CSF-CTCs to determine novel targets for therapy. As a proof of concept, we tested the efficacy of combining ceritinib (cer), an IGF-1R inhibitor and trametinib (tra), a MEK inhibitor, against LMD. METHODS: CSF from 11 pts were collected from various sources (ie: LPs, Ommayas, rapid autopsies). PD-CSF-CTCs were expanded *in vitro* in conditioned media and *in vivo* using cell line-derived xenograft model. Single-cell RNA-sequencing (scRNAseq) analysis was performed to assess transcriptional profiles of PD-CSF-CTCs. RESULTS: Of the total 61 PD-CSF-CTCs collected from 11 pts (avg: 4.07 CSF collections/patient), we successfully cultured PD-CSF-CTCs from 3 pts (20%) and were able to grow them *in vivo* from 2 pts (18%). scRNAseq identified IGF-1R, Sox9, ErbB3 and MLANA were among the enriched genes for PD-CSF-CTCs. IGF-1R inhibition by cer and depletion by CRISPR suppressed cell growth. We evaluated the responses of cer + tra treatment *in vitro* and found that combining these agents produced drug synergy against PD-CSF-CTCs and resensitized BRAF inhibitor-resistant melanoma cell line, WM164R. *In vivo* LMD xenograft model showed cer + tra treatment significantly prolonged median survival of PD-CSF-CTCs LMD (control: 27 days vs treatment: 38.5 days; P value < 0.032) and WM164R LMD (control: 35 days vs treatment: MS not reached; P value < 0.047). CONCLUSIONS: Though the sample size is small, this is the first report of the successful *in vitro* and *in vivo* culture of CSF-CTCs from pts with LMD.