BMET-36. TUMOR PROFILES OF BRAIN METASTASES FROM NSCLC, BREAST CANCER AND MELANOMA
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BACKGROUND: Approximately 70,000 diagnoses of brain metastases (BM) occur annually in the U.S. Despite its prominence, the biology of BM remains poorly understood. We compared tumor profiles of BM from NSCLC, breast cancer (BC) and melanoma (ML) to understand the biology and to identify differential treatment strategies. METHODS: Tumors were profiled using a multiplatform service (Caris Life Sciences, Phoenix, AZ), including sequencing (Sanger, NGS), protein expression (IHC) and amplification (ISH).

RESULTS: 5391 NSCLC (293 BM, 5098 lung), 3595 BC (99 BM, 3496 breast) and 761 ML (101 BM, 660 skin) were included. BM mutations remain largely similar to primary tumors with no consistent changes between cancers. In contrast, when comparing BM to primary tumors, protein expression of TOP2A (NSCLC: 75% vs. 55%; BC: 75% vs. 50%; ML: 76% vs. 46%, all p < 0.01); TOPO1 (64% vs. 55%, p = 0.02; 78% vs. 50%, p < 0.01; 61% vs. 37%, p = ns); TS (35% vs. 22%, p < 0.01, 39% vs. 28%, p = 0.04, 56% vs. 45%, p = ns) and EGFR amplification (36% vs. 28%, p = ns, 31% vs. 14%, p < 0.01; 50% vs. 6%, p < 0.01) were more prevalent in BM.

Higher PD-1 (83% vs. 63%, p = 0.01, 60% vs. 53%, p = ns, 100% vs. 75%, p = ns) expression on TIL was observed in BM; PD-L1 is higher in the BM of NSCLC and BC (22% vs. 16%, p = ns; 40% vs. 12%, p = ns), but not in ML (75% vs. 80%, p = ns). CONCLUSIONS: The mutational landscape is similar in BM of NSCLC, BC and ML compared to primary tumors, suggesting that primary tumor and BM would respond to similar therapeutic agents with the consideration of effective blood-brain-barrier-penetrant drugs. Immune-checkpoint inhibitors could be considered for BM treatment based on PD-1, PD-L1 expression frequencies. Small-molecule EGFR inhibitors could be considered due to increased EGFR amplification; increased TOP2A, TOPO1 expression prompts consideration of topoisomerase inhibitors like etoposide or irinotecan.