until October 2018. We also searched the Chinese databases Wanfang Data, Wanfang Med Online, China National Knowledge Infrastructure, and Chongqing VIP Information for RCTs published until September 2019. Trials including > 10 patients were selected. The primary outcomes were overall survival (OS) and intracranial progression-free survival (PFS). We used a frequentist random-effects model for network meta-analysis and assessed the certainty of evidence using the GRADE approach. RESULTS: Among 8798 abstracts, 106 RCTs (9452 patients) met inclusion criteria. Median sample size was 67 (range 25–554). All trials included adult patients with histologically proven NSCLC and >1 BM proven on CT/MRI. Of trials that reported performance status (e.g. ECOG or KPS, n=67), 63/67 excluded patients with non-favorable performance status. Interventions assessed included surgery, WBRT, SRS, targeted therapies (i.e. EGFR/ALK inhibitors), and chemotherapy. Compared to WBRT alone, several interventions demonstrated a statistically significant increase in median OS, including non-targeted chemotherapy + surgery (MD: 415.3 days, 95% CI: 31.3–799.4), WBRT + EGFRi (MD: 200.2 days, 95% CI:146.3–254.1), and EGFRi alone (MD: 169.7 days, 95% CI: 49.7–289.7). Among all interventions, only WBRT + EGFRi showed a significant improvement in median PFS (MD: 108.0 days, 95%CI: 48.5–167.5). CONCLUSIONS: Our preliminary analyses indicate an OS and PFS benefit on the addition of EGFR inhibitors to WBRT for the treatment of BMs from NSCLC. Further analyses of hazard ratios for OS/PFS are underway, and subgroup analyses are planned. These data support the growing role of targeted therapies in the treatment of BMs, particularly in susceptible mutant tumours.

61. EXPRESSION OF ANDROGEN RECEPTOR IN BREAST CANCER BRAIN METASTASIS

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INTRODUCTION: Treatment options for women with breast cancer brain metastases (BrM) are generally limited to surgery and/or radiotherapy because most systemic therapies do not cross the blood-brain barrier. Androgen receptors (ARs) are frequently expressed in breast cancer and anti-androgenic therapies have been shown to penetrate the central nervous system. In this study, we analyzed the expression of AR in breast cancer BrM to identify patients who may benefit from anti-androgenic therapies. METHODS: Consecutive BrM resected in our institution (July 1999-June 2013) were identified from the Anatomic Pathology departmental database. Cases that were signed out as breast origin given the available immunohistochemical profile and clinical history were included. A tissue microarray was constructed using 1 mm cores in triplicates and studied by immunohistochemistry for AR, ER, PR and HER2 (SP107, SP1, IE2, 4B5; Ventana Medical Systems, Tucson AZ, USA). HER2 gene amplification was determined by INFORM HER2 DNA and Chromosome 17 (both by Ventana Medical Systems, Tucson AZ, USA). Immunohistochemistry was used as a surrogate to determine intrinsic subtypes. RESULTS: Among 61 breast cancer BrM with available tissue blocks, AR was expressed in 38 (62%) cases. Among BrMs of luminal A subtype (ER+, PR+/-, HER2-, Ki67<16%), 50% expressed AR (n=1/2). Within the luminal B subtype (ER+, PR+/-), all 15 HER2+ BrM expressed AR (100%), while only 50% of HER2- BrM expressed AR (n=8/16). Among 14 BrM of HER2+ subtype (ER-, PR-), 71% expressed AR (n=10/14). Only 30% of triple negative BrM (ER-, PR-, HER2-) were AR+ (n=4/14). CONCLUSION: Almost two-thirds of breast cancer BrM expressed AR. HER2+ luminal B and HER2+ subtypes were most likely to be AR+, while only 30% of triple negative BrM were AR+. Our data suggests that certain subtypes of breast cancer BrM are more likely to be AR+ and could serve as a potential therapeutic target.

62. PRESENCE OF EXTRACRANIAL TUMORS INFLUENCES RESPONSE TO IMMUNE CHECKPOINT INHIBITORS IN A PRE-CLINICAL MODEL OF MELANOMA BRAIN METASTASIS

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Up to 75% of patients with melanoma develop brain metastases. While immune checkpoint inhibitors (ICI) targeting PD-1 and CTLA4 have revolutionized the treatment of metastatic melanoma, responses within the immune-specialized microenvironment of the brain are not well understood and there is a paucity of animal models to investigate the effect of ICI intracranially. We characterized responses to checkpoint inhibitors in a syngeneic mouse model of melanoma brain metastasis with concurrent intracranial and subcutaneous melanoma. D3UV3 cells (obtained from David Fisher's laboratory) were derived using UVB irradiation from D4M.3A melanoma cell line and implanted into the striatum using stereotactic injection or subcutaneously injected into the flank of C57BL/6 mice. Mice were then treated with anti-PD-1 antibody, anti-CTLA4 antibody, a combination of anti-PD-1 and anti-CTLA4, or isotype controls. While mice with intracranial melanoma alone had no response to monotherapy with anti-PD-1 or anti-CTLA4 antibody (p=1 and 0.1, respectively), and only a slight response to combination therapy (p=0.049), mice with concurrent subcutaneous tumors had significantly improved responses to anti-PD-1, anti-CTLA4 and combination treatment (p=0.002, 0.01 and 0.01 respectively compared to mice with intracranial tumors alone with equivalent treatment). These results demonstrate that the presence of an extracranial tumor influences response to ICI in pre-clinical mouse models of melanoma brain metastasis. We have therefore established a pre-clinical model with concurrent intracranial and extracranial tumors to better recapitulate the clinically observed context of melanoma brain metastases and lead to a better understanding of the setting in which ICI are effective for patients with this devastating complication.

64. AN ENT2-DEPENDENT, CELL-PENETRATING, AND DNA-DAMAGING LUPUS AUTOANTIBODY CROSSES THE BLOOD-BRAIN BARRIER TO TARGET BRAIN TUMORS

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The blood-brain barrier (BBB) limits conventional antibody-based approaches to brain tumors. ENT2, an equilibrative nucleoside transporter, facilitates penetration of autoantibodies into live cells and is expressed in the BBB. PAT-DX1 (also known as Deoxymab-1 or DX1) is an ENT2-dependent, cell-penetrating, and DNA-damaging lupus autoantibody that is synthetically lethal to cancer cells with defects in the DNA damage response. PTEN loss renders sensitivity to DX1 and is common in primary and metastatic brain tumors. We show that DX1 is toxic to spheroids derived from primary PTEN-deficient glioblastoma (GBM), and crosses the BBB to suppress the growth of orthotopic GBM and breast cancer brain metastases. Mechanistically, we find the ENT2 inhibitor dipyridamole blocks DX1 penetration into brain endothelial cells and transport across the BBB *in vitro* and *in vivo*, consistent with ENT2-mediated uptake of DX1 into brain tumors. Autoantibodies that hijack nucleoside transporters to cross cell membranes may open new frontiers in brain tumor therapy.

65. INVASIVE HISTOPATHOLOGY DRIVES POOR OUTCOMES IN SURGICALLY RESECTED BRAIN METASTASES

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BACKGROUND: Brain metastasis (BrM) patients treated with surgery and radiotherapy frequently experience local recurrence (LR), leptomeningeal metastasis (LM), and poor overall survival (OS). We sought to correlate the presence of invasive or circumscribed histopathological growth pattern, observed in the BrM lesion and surrounding brain, with these outcomes, and to study molecular mediators of parenchymal invasion. METHODS: We assessed the HGP of H&E-stained slides from 164 surgically resected BrM from 147 patients. HGP was correlated with incidence of LR, LM and OS. Single-cell RNA sequencing (scRNAseq) was performed on three invasive HGP patients, sampling the metastasis center (MC) and surrounding brain (SB) outside of the contrast-enhancing region. Orthotopic patient-derived xenograft models (OPDX) were established from N=30 brain metastasis via intracranial propagation. RESULTS: 56/164 BrM specimens (34%) showed a circumscribed growth pattern between the tumor and adjacent brain (cHGP) while 108/164 (66%) showed significant invasion of tumor lobules or single cells into the brain parenchyma (iHGP). iHGP was associated with LR, LM and shortened OS in BrM patients. OPDX models of BrM retain features of patient BrM, including HGP. scRNAseq identified abundant cancer cells in SB that overexpressed a number of genes involved in cell survival, invasion and metastasis compared to matched cancer cells in MC. Validation of these targets with immunohistochemistry in patient and OPDX tissues revealed cold-inducible RNA binding protein (CIRBP) overexpression in iHGP patient and OPDX BrM. Modulation of CIRBP expression in OPDX and cell line models of iHGP BrM delayed BrM progression and extended OS. CONCLUSION: iHGP is a poor prognostic indicator in patients with surgically resected BrM, establishing HGP as an