PM-19. DEVELOPMENT OF A PANEL OF PATIENT-DERIVED XENOGRAFT (PDX) MODELS FROM BRAIN METASTASES
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BACKGROUND: Most common models of brain metastases are developed from established cell lines selected for brain tropism. We hypothesized that PDX models derived from brain metastases would maintain brain tropism and more faithfully maintain features of primary brain metastases.

METHODS: Resected brain metastases were used to establish PDX models. Survival was assessed following intracranial or intracardiac injection of explant cultures. Radiation response was assessed using 20 Gy in 5 fractions.

RESULTS: From January 1, 2013 to May 31, 2014, 41 brain metastases from 40 patients were implanted into athymic mice, and 25 of 34 (74%) models implanted more than 3 months ago could be serially transplanted. These include 9 melanoma, 7 non-small lung (NSCLC), 1 small-cell lung, 4 gastro-intestinal (pancreas, esophagus, colorectal), and 2 breast cancers. Intracardiac injection of 1E5 cells resulted in consistent development of multiple brain metastases in models from NSCLC (M5), melanoma (M2, M12, M15), but not esophageal (M7). In a titration study, intracardiac injection of 1E5, 1E4, and 1E3 cells resulted in a median survivals of: M12 - 31, 59, and 167 days; M15 - 70, 107 and 192 days, respectively. Direct intracranial injection of tumor cells resulted in large, unifocal brain tumors with histology similar to the original patient tumor. Median survivals were: M1 - 63 days, M2 - 46 days, M5 - 12 days, M7 - 43, M15 - 10 days, M20 - 14 days. Using established intracranial tumors, radiation significantly extended survival compared to sham irradiation in breast (M1: median survival >132 vs. 48 days) and esophageal (M7: 75 vs. 43 days) models but not in melanoma models (M2: 52 vs. 52 days; M12, 22 vs. 18 days). CONCLUSIONS: These brain metastasis PDX models may be useful for basic mechanistic studies of metastatic behavior and translational studies of novel therapeutic strategies.