AB024. S024. Drug responses of patient-derived cell lines *in vitro* that match drug responses of patient PDAc tumors *in situ*

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Abstract: Pancreatic ductal adenocarcinoma (PDAC) is a devastating disease for which the incidence and mortality rates are nearly equivalent. Only 2% of patients with metastatic disease survive 5 years after diagnosis. Even in rare cases of partial response to systemic chemotherapy, disease typically recurs and the National Comprehensive Cancer Network (NCCN) guidelines recommend clinical trials as the next best option. Outcomes are more promising if tumors are confined to the pancreas and can be surgically resected; yet only 20% of patients treated surgically are disease free after 5 years. Approximately 30% of patients diagnosed with metastatic PDAC have partial responses to modern standard-of-care (SOC) chemotherapy regimens, though these responses are typically short-lived. However, exceptional cases of durable response to chemotherapy do exist and understanding the nature of these chemo-sensitive tumors may reveal biomarkers of tumor susceptibility to chemotherapy. Moreover, no biomarker exists to guide selection of SOC FOLFIRINOX or gemcitabine + Abraxane regimens, and chance dictates response even though one regimen may be significantly more effective. Clinical trials using biomarker-guided, targeted therapeutics have not typically demonstrated efficacy over SOC chemotherapy. Given these findings it is important to identify which SOC chemotherapy regimen will be most effective against PDAC. We have identified PDAC tumors which were exceptionally sensitive to SOC chemotherapy *in situ* and used biopsied or resected tumor tissue to generate low-passage, continuously-regenerating cell lines (CRCs). We collected over 100 treatment-naïve tumor specimens and then tracked future responses to SOC chemotherapy to identify exceptionally chemo-sensitive CRCs. We found strong concordance between the *in situ* tumor response and the *in vitro* CRC responses to SOC agents. We performed a real-time, multimetric in vitro drug-response assay designed to measure growth rate, time and concentration required for drug-induced cell death, and the ability of CRCs to proliferate after drug withdrawal. Results from the multimetric, drug-response assay identified parameters other than conventional endpoint metrics (e.g., IC50) that best matched the known *in situ* response. By understanding the *in vitro* cell behaviors that reflect *in situ* tumor sensitivity we hope to identify biomarkers that can be used to guide drug selection in patients diagnosed with PDAC.

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