

A 45-Year Experience with Abdominal Melanoma Metastases: Is Surgical Cure Still Relevant in the Era of Modern Systemic Therapy?

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INTRODUCTION: Although systemic therapies for metastatic melanoma have evolved rapidly over the last decade, no large study has yet examined the relative impact of surgical resection for abdominal metastases in this setting.

METHODS: We examined our records for melanoma patients diagnosed with potentially resectable abdominal metastases before (1969-2001) and after (2002-2014) recent advances in systemic therapies to determine the survival impact of surgical treatment and metastatic site. Multivariable regression analysis included age, sex, primary tumor characteristics, regional nodal status, abdominal metastasis-free interval, and treatment era.

RESULTS: Of 5,668 patients with metastatic melanoma, 1,317 (23%) had abdominal metastases (gastrointestinal [GI] tract [n=336], liver [n=697], adrenal glands [n=137], pancreas [n=38], and spleen [n=109]). Median follow-up was 43 months. Among patients with GI tract, liver, and splenic involvement, overall survival (OS) rates were higher in the surgical (n=308) vs non-surgical (n=1,009) patients (p<0.01); clinicopathologic characteristics did not significantly differ. In the surgical patients, lack of ulceration (p=0.02; hazard ratio [HR] 0.57), decreasing Breslow thickness (p=0.01; HR 0.86), and longer abdominal metastasis-free interval from primary diagnosis (p=0.03; HR 0.99) all predicted better OS; treatment era and metastatic site did not affect survival. Patients undergoing complete curative resection had the greatest benefit.

CONCLUSIONS: This series, which, to our knowledge, is the largest single-institution experience with abdominal melanoma metastases, demonstrates that surgical resection offers the best opportunity for long-term survival, independent of modern systemic treatment.

A Metabolomics-Based Understanding of Pro-Tumorigenic Hypoxia Inducible Factor-1 α Activity in Pancreatic Cancer and Local Macrophages

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INTRODUCTION: Metabolomics compares metabolite profiles to understand metabolic processes contributing to pathologic conditions. Numerous metabolic changes are found in tumor cells, including increased glycolysis, reduced reliance on the tricarboxylic acid (TCA) cycle, and increased polyamine

metabolism. These collectively contribute to tumor growth, invasion, and macrophage activation. Increased lactate production and glycolysis specifically are mediated in part by hypoxia inducible factor-1 α (HIF1 α). We showed that murine pancreatic tumor-derived HIF1 α affects macrophage activation. We further hypothesized that tumor-derived HIF1 α alters macrophage metabolism.

METHODS: Wild-type (WT) Pan02 murine pancreas adenocarcinoma cells were modified to create Pan02/HIF1 α - cells lacking HIF1 α . Wild-type and HIF1 α - cell lines were used to produce a cancer-conditioned media (CCM) rich in tumor-derived factors. Murine macrophages were exposed to CCM from both lines, generating cancer-activated macrophages (CAMs). Tumor cells and CAMs underwent metabolomic analysis using ultra-performance liquid chromatography/mass spectrometry.

RESULTS: Pan02/HIF1 α - cells had decreased consumption of glycolysis metabolites (p<0.001), with increased consumption of TCA cycle metabolites (p=0.003). Additionally, Pan02/HIF1 α - cells had less polyamine production than WT Pan02 cells (p<0.001). Wild-type Pan02-exposed CAMs had increased glycolysis (p=0.0184), TCA cycle activity (p=0.0130), arginine uptake (p=0.00543), and polyamine production (p<0.0001). The CAMs exposed to Pan02/HIF1 α - CCM had decreased glycolysis (p=0.00343), lactate (p=0.00153), and TCA cycle activity (p=0.00822).

CONCLUSIONS: Inhibition of HIF1 α reduced tumor glycolysis and polyamine production, with consequent increased TCA cycle activity. Furthermore, tumor HIF1 α inhibition reduced the immunologic activity of cancer-activated macrophages via decreased glycolysis, arginine uptake, and polyamine generation. Therefore, targeting HIF1 α therapeutically may metabolically inhibit tumorigenesis via decreased glycolysis, polyamine generation, and macrophage activation.

Cancer Survivorship: Defining the Incidence of Incisional Hernia After Resection for Intra-abdominal Malignancy

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INTRODUCTION: Cancer survivorship focuses on minimizing adverse consequences of cancer and treatment while improving quality of life (QOL). We aimed to determine the rate of ventral incisional hernia (VIH) formation after cancer resection, with implications for survivorship.

METHODS: We followed patients without previous history of VIH or VIH repair, who underwent abdominal operations for malignancy between January 1, 2008, and December 31, 2009, at a tertiary center. Patients were included if they had a viewable