

In Vitro Chemotherapy Profiling of Well-Differentiated Midgut Neuroendocrine Tumors (NETs) Based on Individual Patient Tumor Biomarkers Analysis

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Background: Midgut neuroendocrine tumors (NETs) are rare malignancies with indolent clinical courses. In general, they are well differentiated with most tumor cells in the G0 phase of the cell cycle, consistent with the poor response rate of NETs to chemotherapy in vivo. We hypothesize that insults, such as surgery, can drive NET cells from G0 into S phase and that biomarker analysis of individual patient tumors harvested and grown in the lab will provide useful practical guide for future intra and post operative adjuvant therapy.

Methods: 97 well-differentiated midgut NET patients underwent cytoreductive surgery at our institution between 5/2012 and 10/2012. 148 surgical specimens were collected and submitted to a single commercial lab for processing. Primary tumors, lymph nodes and liver metastases were harvested and cultured. Their RNAs were then extracted to analyze the expressivity a total of 88 different biomarkers. Based on our patients specific tumor biomarker expressivity and known correlations between 36 anti-neoplastic agents with their linked biomarkers, recommendations were reported as clinically benefit or lacking such benefit.

Results: A total of 148 specimens from 97 patients were tested. In four of the 97 patients, no clinically beneficial chemotherapy agent could be identified. Among the remaining 93 patients, the top three agents that are most likely to be clinically beneficial are: Fluorouracil, Cisplatin and Carboplatin. These were reported to be clinically beneficial in 135/148 (91.2%), 103/148 (69.6%), and 103/148 (69.6%) patients respectively.

Conclusions: Midgut NETs are slow growing tumors which are chemotherapeutically inert owing to the fact that most of the tumor cells are in G0 cell cycle. Surgical insult drives NET cells into active synthetic phase where they begin to express biomarkers specific to their tumor cells. Analysis of these biomarkers guides further potential beneficial therapy based on the current known associations among biomarkers and chemotherapy agents. These results must then be compared and confirmed against a direct in-vitro chemo sensitivity assessment conducted simultaneously on the same patients.