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Use of Molecular Profiling to Guide Treatment Decisions in Patients with Neuroendocrine Tumors

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Background: Neuroendocrine tumors (NETs) constitute a rare orphan disease. As their incidence continues to increase, so does the need for effective treatments. Various cytotoxic and targeted therapies have had low response rates in trials, with a few exceptions. Predictive markers for specific therapies measured by molecular profiling of resected tumor tissue could potentially improve selection of treatments and lead to better responses.

Methods: Resected carcinoid tumor samples at one institution were sent for molecular profiling over a 3-year period. Molecular profiling tests were ordered to measure the expression of twenty proteins and oncogenes using immunohistochemical staining, gene sequencing, and fluorescent in-situ hybridization. Potentially beneficial systemic therapies were identified by comparing these biomarker levels against a comprehensive review of the chemotherapy response literature. The clinical charts of 41 patients who underwent molecular profiling and treatment from 2010 to 2012 were reviewed retrospectively, and 12 were selected for our case series to represent the range of effects molecular profiling has had on carcinoid treatment. Their presentation, molecular profile results, treatment, and disease progression is reviewed in the following case series.

Results: A total of 9 patients in this series were treated with drugs identified as potentially beneficial by molecular profile reports. These drugs include capecitabine, 5-fluorouracil, temozolomide, oxaliplatin, and gemcitabine. Based on clinical symptoms, serum markers of disease, and radiographic evidence 5 of 9 patients responded to treatment, 2 had mixed responses, and 2 did not respond to treatment. Grade 3 NETs do not appear to be well suited for treatment guided by molecular profiling at this time.

Conclusion: At this early juncture, our critique of molecular profiling for neuroendocrine tumors is favorable, as a significant number of our patients responded to drugs identified by molecular profiling as potentially beneficial.

Table 1 – Treatments and Responses

Patient	Primary Tumor Site	Treatment Selected from Molecular Profile Report?	Treatment*	Response
1	Lung	Yes	CAPTEM	Good
2	Small Bowel	Yes	Capecitabine	Good
3	Lung	No	Everolimus	Good
4	Lung	No	Etoposide + Cisplatin	Good
5	Lung	Yes	Gemcitabine	Good
6	Pancreas	Yes	CAPTEM	Good
7	Small Bowel	No	Everolimus	Good
8	Small Bowel	Yes	CAPTEM	Mild
9	Small Bowel	Yes	5-FU	None
10	Small Bowel	Yes	Temozolomide	None
11	Small Bowel	Yes	CAPTEM	Good
12	Small Bowel	Yes	CAPTEM	Mixed

Abbreviations: CAPTEM = capecitabine + temozolomide, 5-FU = 5-fluorouracil

* Multiple treatments may have been tried for a given patient; however, Table 1 lists only the treatments indicated by molecular profile that elicited the greatest response.